12/12/04 10/764,853

STRUCTURE FILE UPDATES: 10 DEC 2004 HIGHEST RN 796738-17-5
DICTIONARY FILE UPDATES: 10 DEC 2004 HIGHEST RN 796738-17-5

TSCA INFORMATION NOW CURRENT THROUGH MAY 21 2004

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Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at: http://www.cas.org/ONLINE/DBSS/registryss.html

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COST IN U.S. DOLLARS SINCE FILE ENTRY TOTAL SESSION
FULL ESTIMATED COST 0.42 0.63

FILE 'CAPLUS' ENTERED AT 22:25:43 ON 12 DEC 2004
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FILE COVERS 1907 - 12 Dec 2004 VOL 141 ISS 25
FILE LAST UPDATED: 10 Dec 2004 (20041210/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s 522615-02-7/rn
1 522615-02-7
0 522615-02-7D
L1 1 522615-02-7/RN
(522615-02-7 (NOTL) 522615-02-7D)

=> d L1

L1 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:376836 CAPLUS
DN 138:368886
TI Preparation of 4-(azinylmethyl)-substituted 2-aminothiazoline derivatives as inhibitors of inducible NO-synthase and their use in the treatment of Parkinson's disease
IN Bigot, Antony; Carry, Jean-Christophe; Mignani, Serge
PA Aventis Pharma S.A., Fr.
SO PCT Int. Appl., 26 pp.
CODEN: PIXXD2
DT Patent
LA French

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FAN.CNT 1
     PATENT NO.            KIND   DATE        APPLICATION NO.          DATE
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PI   WO 2003040115          A1    20030515    WO 2002-FR3810           20021107
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             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
             PL, PT, RO, RU, SC, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT,
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             CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
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             NE, SN, TD, TG
     FR 2832152              A1    20030516    FR 2001-14510            20011109
     BR 2002006354           A     20031223    BR 2002-6354             20021107
     EP 1446393              A1    20040818    EP 2002-796839           20021107
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK
     US 2003166646           A1    20030904    US 2002-291084           20021108
     US 6699867              B2    20040302
     NO 2003003129           A     20030827    NO 2003-3129             20030708
     US 2004157843           A1    20040812    US 2004-764853           20040126
PRAI FR 2001-14510           A     20011109
     US 2002-352797P         P     20020130
     WO 2002-FR3810          W     20021107
     US 2002-291084          A1    20021108
OS   MARPAT 138:368886
RE.CNT  4     THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
              ALL CITATIONS AVAILABLE IN THE RE FORMAT


=> s 522615-10-7/rn
             1 522615-10-7
             0 522615-10-7D
L2           1 522615-10-7/RN
                 (522615-10-7 (NOTL) 522615-10-7D )

=> d L2

L2   ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2004 ACS on STN
AN   2003:376836  CAPLUS
DN   138:368886
TI   Preparation of 4-(azinylmethyl)-substituted 2-aminothiazoline derivatives
     as inhibitors of inducible NO-synthase and their use in the treatment of
     Parkinson's disease
IN   Bigot, Antony; Carry, Jean-Christophe; Mignani, Serge
PA   Aventis Pharma S.A., Fr.
SO   PCT Int. Appl., 26 pp.
     CODEN: PIXXD2
DT   Patent
LA   French
FAN.CNT 1
     PATENT NO.            KIND   DATE        APPLICATION NO.          DATE
     ---------------       ----   --------    --------------------     --------
PI   WO 2003040115          A1    20030515    WO 2002-FR3810           20021107
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             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
             PL, PT, RO, RU, SC, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT,
             TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ,
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     Pyrimidinetrione, derivs.   12794-10-4D, Benzodiazepine, derivs.
     RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
        (dependence on; preparation of triazatetracycloentaene succinate for
        pharmaceutical compns.)
IT   535959-68-3P
     RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); THU
     (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT
     (Reactant or reagent); USES (Uses)
        (preparation of triazatetracycloentaene succinate for pharmaceutical
        compns.)
IT   535959-69-4P
     RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use);
     BIOL (Biological study); PREP (Preparation); USES (Uses)
        (preparation of triazatetracycloentaene succinate for pharmaceutical
        compns.)
IT   249296-44-4
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (preparation of triazatetracycloentaene succinate for pharmaceutical
        compns.)


=> s piperazin? and "1,3-thiazol?"
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       6181361 "3"
          2224 "THIAZOL"
            10 "THIAZOLS"
          2233 "THIAZOL"
                 ("THIAZOL" OR "THIAZOLS")
           487 "1,3-THIAZOL?"
                 ("1"(W)"3"(W)"THIAZOL")
L7          112 PIPERAZIN? AND "1,3-THIAZOL?"

=> s huntington?(2a)chorea
          5362 HUNTINGTON?
          4368 CHOREA
             8 CHOREAS
          4371 CHOREA
                 (CHOREA OR CHOREAS)
L8          4124 HUNTINGTON?(2A)CHOREA

=> s L7 and L8
L9             5 L7 AND L8

=> d L9 ibib abs 1-5

L9   ANSWER 1 OF 5  CAPLUS  COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER:         2004:550745  CAPLUS
DOCUMENT NUMBER:          141:106475
TITLE:                    Preparation of 5-membered heterocycle derivatives for
                          treating neurodegenerative disorders or pain
INVENTOR(S):              Chabrier De Lassauniere, Pierre-Etienne; Harnett,
                          Jeremiah; Bigg, Dennis; Liberatore, Anne-Marie;
                          Pommier, Jacques; Lannoy, Jacques; Thurieau,
                          Christophe
PATENT ASSIGNEE(S):       USA
SOURCE:                   U.S. Pat. Appl. Publ., 150 pp., Cont.-in-part of U.S.
                          Ser. No. 89,993.
                          CODEN: USXXCO
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   2
PATENT INFORMATION:
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PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004132788	A1	20040708	US 2003-681002	20031008
FR 2799461	A1	20010413	FR 1999-12643	19991011
FR 2799461	B1	20020104		
FR 2812546	A1	20020208	FR 2000-10151	20000801
WO 2001026656	A2	20010419	WO 2000-FR2805	20001010
WO 2001026656	A3	20020418		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

EP 1228760	A2	20020807	EP 2002-76763 20001010
EP 1228760	A3	20040128	

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL

PRIORITY APPLN. INFO.:

FR 1999-12643	A	19991011
FR 2000-10151	A	20000801
FR 2000-11169	A	20000901
WO 2000-FR2805	W	20001010
JP 1989-4943	A	20010410
JP 1990-1811	A	20020214
US 2002-89993	A2	20020404
EP 2000-967988	A3	20001010

OTHER SOURCE(S): MARPAT 141:106475

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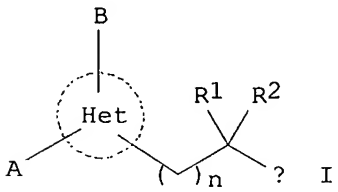

AB The invention relates to thiazole, oxazole, imidazole, isoxazole and isoxazoline derivs. of general formula (I) [wherein Het = thiazole, oxazole, imidazole, isoxazole or isoxazoline; n = an integer from 0 to 6; A = optionally substituted aromatic radical; B = H, alkyl, Ph; R1, R2 = H, alkyl, cycloalkyl; Ω = NR46R47 or OR48; R46, R47 = H, alkyl, cycloalkyl, (CH2)k-CO2R51; R51 = alkyl, haloalkyl; R48 = H, alkyl]. These compds. have advantageous pharmacol. properties which allow their use in a medicament intended to inhibit monoamine oxidases (MAO) and/or lipidic peroxidn. and/or to act as modulators of the sodium channels and notably their use in therapeutics for treating (1) central or peripheral nervous system, (2) neurodegenerative disorders selected from Parkinson's disease, Alzheimer's disease, **Huntington's chorea** and amyotrophic lateral sclerosis or (3) pain selected from the group consisting of postoperative pain, migraine, neuropathic pain, central pain, chronic inflammatory pain and pain linked to a cancer. Thus, 2-[[[(1,1-dimethylethoxy)carbonyl]methyl]amino]ethanethioamide (4.3 g, 2.11 mmol) and 2-bromo-1-(3,5-di-tert-butyl-4-hydroxyphenyl)ethanone (6,9 g, 2,11 mmol) were dissolved in 75 mL benzene under argon atmospheric and stirred

at ambient temperature for 12 h to give, after workup and silica gel chromatog.,
4-[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]-N-[(1,1-dimethylethoxy)carbonyl]-N-methyl-2-thiazolemethanamine which was treated with CF3CO2H and triethylsilane in 50 mL CH2Cl2 to give, after workup, 4-[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]-N-methyl-2-thiazolemethanamine (II). II showed IC50 of lower than 10 μM for inhibiting lipid peroxidn. of the cerebral cortex of rats.

L9 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:319488 CAPLUS
DOCUMENT NUMBER: 138:337988
TITLE: Novel 2-[(iminomethyl)amino]phenyl derivatives useful as inhibitors of NO synthase and lipid peroxidation, their preparation, their application as medicines, and pharmaceutical compositions containing them
INVENTOR(S): Chabrier De Lassauniere, Pierre Etienne; Auvin, Serge; Bigg, Dennis; Auguet, Michel; Harnett, Jeremiah
PATENT ASSIGNEE(S): Societe de Conseils de Recherches et D'Applications scientifiques (S.C.R.A.S.), Fr.
SOURCE: U.S. Pat. Appl. Publ., 78 pp., Cont.-in-part of U.S. Ser. No. 882,264.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003078420	A1	20030424	US 2002-191950	20020709
US 6809088	B2	20041026		
FR 2761066	A1	19980925	FR 1997-3528	19970324
FR 2761066	B1	20001124		
FR 2764889	A1	19981224	FR 1997-7701	19970620
FR 2764889	B1	20000901		
WO 9842696	A1	19981001	WO 1998-FR288	19980216
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RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
WO 9858934	A1	19981230	WO 1998-FR1250	19980615
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US 6335445	B1	20020101	US 1999-456205	19991207
US 2002007062	A1	20020117	US 2001-882264	20010615
US 6630461	B2	20031007		

PRIORITY APPLN. INFO.:

FR 1997-3528	A	19970324
FR 1997-7701	A	19970620
WO 1998-FR288	W	19980216
WO 1998-FR1250	W	19980615
US 1999-456205	A3	19991207
US 2001-882264	A2	20010615

US 1999-381749 A2 19990922

OTHER SOURCE(S): MARPAT 138:337988
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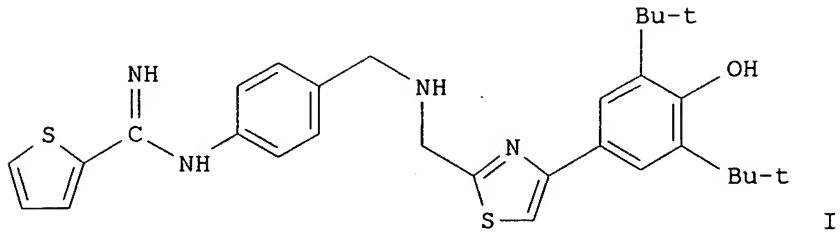

I

AB Title compds., e.g., N-[4-[[[[4-(3,5-di-tert-butyl-4-hydroxyphenyl)-**1,3-thiazol**-2-yl]methyl]amino]methyl]phenyl]th iophene-2-carboximidamide (I) are prepared The compds. are inhibitors of NO synthases, and are also antioxidants which inhibit lipid peroxidn. Approx. 70 examples are prepared I had IC50 for inhibiting rat neuronal NO synthase in vitro < 3.5 μM, and the IC50 for inhibiting rat cerebral lipid peroxidn. in vitro is < 30 μM.

L9 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:814116 CAPLUS
DOCUMENT NUMBER: 137:325417
TITLE: Preparation and application of 5-membered heterocycles as medicaments
INVENTOR(S): Harnett, Jeremiah; Bigg, Dennis; Liberatore, Anne-Marie; Rolland, Alain
PATENT ASSIGNEE(S): Societe De Conseils De Recherches Et D'applications Scientifiques (SCRAS), Fr.
SOURCE: PCT Int. Appl., 132 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002083656	A2	20021024	WO 2002-FR1218	20020409
WO 2002083656	A3	20030103		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
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FR 2823208	A1	20021011	FR 2001-4943	20010410
FR 2823208	B1	20040319		
CA 2443403	AA	20021024	CA 2002-2443403	20020409
EP 1379514	A2	20040114	EP 2002-761921	20020409
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JP 2004531526	T2	20041014	JP 2002-581412	20020409

NO 2003004524	A	20031029	NO 2003-4524		20031009
PRIORITY APPLN. INFO.:			FR 2001-4943	A	20010410
			FR 2002-1811	A	20020214
			WO 2002-FR1218	W	20020409

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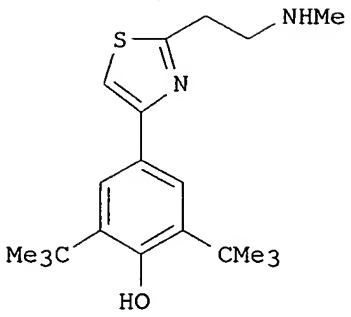

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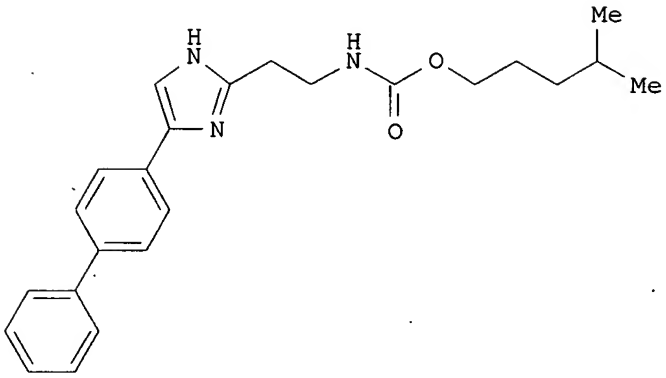

II

AB The invention relates to thiazole, oxazole or imidazole derivs. having at least one of the following pharmacol. activities:: inhibition of monoamine oxydases (MAO); inhibition of lipid peroxidn.; modulation of sodium channels. The inventive compds. comprise, for example, 2,6-di(tert-butyl)-4-{2-[2-(methylamino)ethyl]-**1,3-thiazol**-4-yl}phenol (I); and 4-methylpentyl 2-[4-(1,1'-biphenyl-4-yl)-1H-imidazol-2-yl]ethyl carbamate (II). Thus, I·HCl was prepared from N-methyl-β-alaninenitrile via. N-protection with (Boc)2O in CH2Cl2 containing EtN(CHMe2)2, sulfurization with H2S in EtOH containing Et3N, cyclocondensation with α-bromo-1-[3,5-di(tert-butyl)-4-hydroxyphenyl]ethanone and acid-catalyzed deprotection with HCl in EtOAc. By virtue of their pharmacol. properties, said compds. can be used to treat one of the following disorders or diseases: Parkinson's disease, senile dementia, Alzheimer's disease, **Huntington**'s **chorea**, amyotrophic lateral sclerosis, schizophrenia, depression, psychoses, migraine or pain, especially neuropathic pain. The pharmacol. activity of I was determined [CI50 ≤ 10 μM vs. monoamine oxydase B; CI50 ≤ 10 μM vs. lipid peroxidn.; CI50 ≤ 1.0 μM on sodium channels from the cerebral cortex of rats].

L9 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:	2002:107318 CAPLUS
DOCUMENT NUMBER:	136:151163
TITLE:	Preparation of indazole derivatives as JNK enzyme inhibitors
INVENTOR(S):	Bhagwat, Shripad S.; Satoh, Yoshitaka; Sakata, Steven T.
PATENT ASSIGNEE(S):	Signal Pharmaceuticals, Inc., USA

SOURCE: PCT Int. Appl., 412 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002010137	A2	20020207	WO 2001-US23890	20010730
WO 2002010137	C2	20030206		
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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
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EP 1313711	A2	20030528	EP 2001-957332	20010730
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NZ 524045	A	20040730	NZ 2001-524045	20010730
PRIORITY APPLN. INFO.:			US 2000-221799P	P 20000731
			WO 2001-US23890	W 20010730

OTHER SOURCE(S): MARPAT 136:151163

AB Indazole derivs., 3-R1A-5-R2-1H-indazoles (1), having activity as selective inhibitors of JNK are disclosed. In 1: A is a direct bond, -(CH2)a-, -(CH2)bCH:CH(CH2)c-, or -(CH2)bC.tplbond.C(CH2)c-; R1 is aryl, heteroaryl or heterocycle fused to Ph, each being optionally substituted with 1-4 R3; R2 is -R3, -R4, -(CH2)bC(O)R5, -(CH2)bC(:O)OR5, -(CH2)bC(O)NR5R6, -(CH2)bC(O)NR5(CH2)cC(O)R6, -(CH2)bNR5C(O)R6, -(CH2)bNR5C(O)NR6R7, -(CH2)bNR5R6, -(CH2)bOR5, -(CH2)bSOdR5 or -(CH2)bSO2NR5R6. A is 1-6; b and c are the same or different and are 0-4; d is 0-2. R3 is at each occurrence independently halogen, hydroxy, carboxy, alkyl, alkoxy, haloalkyl, acyloxy, thioalkyl, sulfinylalkyl, sulfonylalkyl, hydroxyalkyl, aryl, substituted aryl, arylalkyl, substituted arylalkyl, heterocycle, substituted heterocycle, heterocyclealkyl, substituted heterocyclealkyl, -C(O)OR8, -C(O)R8, -C(O)NR8R9, -C(O)NR8OR9, -SO2NR8R9, -NR8SO2R9, -CN, -NO2, -NR8R9, -NR8C(O)R9, -NR8C(O)(CH2)bOR9, -NR8C(O)(CH2)bR9, -O(CH2)bNR5R9, or heterocycle fused to Ph. R4 is alkyl, aryl, arylalkyl, heterocycle or heterocyclealkyl, each being optionally substituted with 1-4 R3, or R4 is halogen or hydroxy. R5, R6and R7 are the same or different and are H, alkyl, aryl, arylalkyl, heterocycle or heterocyclealkyl, wherein each of R5, R6 and R7 are optionally substituted with 1-4 R3. R8 and R9 are the same or different and at each occurrence independently H, alkyl, aryl, arylalkyl, heterocycle, or heterocyclealkyl, or R8 and R9 taken together with the atom or atoms to which they are bonded form a heterocycle, wherein each of R8, R9, and R8 and R9 taken together to form a heterocycle are optionally substituted with 1-4 R3 with the proviso that: when A is a direct bond and R1 is Ph, R2 is not Me, methoxy, C(O)CH3 or C(O)H; when A is a direct bond and R1 is 4-Me-Ph, R2 is not Me; when A is a direct bond and R1 is 4-F-Ph, R2 is not trifluoromethyl; when A is a direct bond or -C.tplbond.C- and R1 is Ph, R2 is not -COOEt; and when A is a direct bond and R1 is 6,7-dimethoxyisoquinolin-1-yl, R2 is not hydroxy. Such compds. have utility in the treatment of a wide range of conditions that are responsive to JNK inhibition. Thus, methods of treating such conditions are also disclosed, as are pharmaceutical compns. containing one or more compds. of the above compds. Many of the claimed compds. have IC50 values

≤0.5 μM in the JNK2 assay, e.g. 5-[3-(4-fluorophenyl)-1H-indazol-5-yl]-2H-1,2,3,4-tetrazole. Although the methods of preparation are not claimed, >400 example prepns. are included.

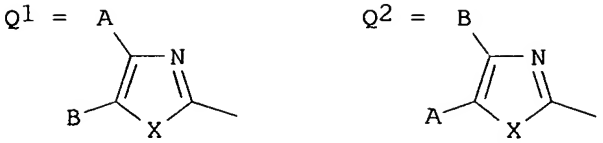
L9 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:283789 CAPLUS
DOCUMENT NUMBER: 134:311210
TITLE: 5-Membered heterocycle derivatives useful as monoamine oxidase inhibitors, lipid peroxidation inhibitors, and sodium channel modulators, and the production thereof, and use thereof as medicaments
INVENTOR(S): Chabrier de Lassauniere, Pierre-Etienne; Harnett, Jeremiah; Bigg, Dennis; Pommier, Jacques; Lannoy, Jacques; Liberatore, Anne-Marie; Thurieau, Christophe
PATENT ASSIGNEE(S): Societe de Conseils de Recherches et d'Applications Scientifiques (S.C.R.A.S, Fr.
SOURCE: PCT Int. Appl., 261 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

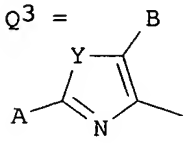
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001026656	A2	20010419	WO 2000-FR2805	20001010
WO 2001026656	A3	20020418		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
FR 2799461	A1	20010413	FR 1999-12643	19991011
FR 2799461	B1	20020104		
FR 2812546	A1	20020208	FR 2000-10151	20000801
CA 2388505	AA	20010419	CA 2000-2388505	20001010
BR 2000014649	A	20020618	BR 2000-14649	20001010
EP 1223933	A2	20020724	EP 2000-967988	20001010
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
EP 1228760	A2	20020807	EP 2002-76763	20001010
EP 1228760	A3	20040128		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
JP 2003511416	T2	20030325	JP 2001-529718	20001010
NZ 518304	A	20040730	NZ 2000-518304	20001010
NO 2002001689	A	20020530	NO 2002-1689	20020410
US 2004132788	A1	20040708	US 2003-681002	20031008

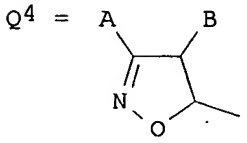
PRIORITY APPLN. INFO.:

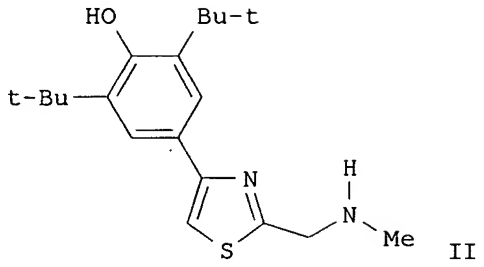
FR 1999-12643	A	19991011
FR 2000-10151	A	20000801
FR 2000-11169	A	20000901
EP 2000-967988	A3	20001010
EP 2002-76763	A3	20001010
WO 2000-FR2805	W	20001010
JP 1989-4943	A	20010410
JP 1990-1811	A	20020214
US 2002-89993	A2	20020404

OTHER SOURCE(S): MARPAT 134:311210
GI









II

AB The invention relates to pharmaceutical use of heterocyclic compds. of general formula Het(A)(B)-(CH2)n-CR1R2-Q [I; wherein the substituted heterocyclic ring Het(A)(B) = Q1-Q4; A = various aryl or heteroaryl systems, especially a substituted Ph or biphenyl radical, or also alkyl, cycloalkyl, or cycloalkylalkyl; B = especially H or alkyl, or also aryl or substituted alkyl; X = especially NH or S, or also substituted NH; Y = O or S; n = 0-6; R1, R2 = especially H, alkyl, or cycloalkyl; Q = NR3R4 or OR5; R3 and R4 = especially H, alkyl, cycloalkyl, alkynyl, cyanoalkyl alkoxycarbonyl, aralkoxycarbonyl or (cycloalkyl)oxycarbonyl; R5 = H, alkyl, alkynyl, or cyanoalkyl]. I and their racemates, enantiomers, and/or salts can be used for producing medicaments for inhibiting monoamine oxidases (MAO), inhibiting lipid peroxidn., and/or for acting as modulators of sodium channels. The resulting medicaments are particularly for use in treating Parkinson's disease, senile dementia, Alzheimer's disease, **Huntington**'s **chorea**, amyotrophic lateral sclerosis, schizophrenia, depression, psychosis, pain and epilepsy. Approx. 350 synthetic examples of I and their salts are given, and numerous free bases of I are claimed. For instance, protection of sarcosinamide-HCl with BOC anhydride gave 72% BOC-N(Me)CH2CONH2, which was converted to the thioamide with (P2S5)2 in 65% yield. Cyclocondensation of the thioamide with 2-bromo-1-(3,5-di-tert-butyl-4-hydroxyphenyl)ethanone (28%), followed by deprotection (73%) and salification (92%), gave thiazole derivative II as the HCl salt. II inhibited binding of the MAO-B specific ligand [3H]-Ro-19-6327 to rat mitochondrial prepns. with IC50 < 10 μM. Selected I also inhibited formation of malondialdehyde by lipid peroxidn. in rat cerebral cortex prepns., and inhibited specific binding of [3H]-batrachotoxin to voltage-dependent sodium channels in rat cerebral cortex homogenates.

=> s ?morpholin? and "?1,3-thiazol?"
67926 ?MORPHOLIN?

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       8112958 "1"
       6181361 "3"
          2224 "THIAZOL"
            10 "THIAZOLS"
          2233 "THIAZOL"
                 ("THIAZOL" OR "THIAZOLS")
           487 "?1,3-THIAZOL?"
                 ("1"(W)"3"(W)"THIAZOL")
L10         134 ?MORPHOLIN? AND "?1,3-THIAZOL?"

=> s ?piperazin? and "?1,3-thiazol?"
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       6181361 "3"
          2224 "THIAZOL"
            10 "THIAZOLS"
          2233 "THIAZOL"
                 ("THIAZOL" OR "THIAZOLS")
           487 "?1,3-THIAZOL?"
                 ("1"(W)"3"(W)"THIAZOL")
L11         126 ?PIPERAZIN? AND "?1,3-THIAZOL?"

=> duplicate remove L10,L11
PROCESSING COMPLETED FOR L10
PROCESSING COMPLETED FOR L11
L12         173 DUPLICATE REMOVE L10 L11 (87 DUPLICATES REMOVED)

=> Huntington?(w)chorea
HUNTINGTON?(W)CHOREA IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> s Huntington?(2a)chorea
          5362 HUNTINGTON?
          4368 CHOREA
             8 CHOREAS
          4371 CHOREA
                 (CHOREA OR CHOREAS)
L13       4124 HUNTINGTON?(2A)CHOREA

=> L12 and L13
L12 IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> s L12 and L13
L14         134 S L12
L15          39 S L12
L16           7 (L14 OR L15) AND L13

=> d L16 ibib abs 1-7

L16  ANSWER 1 OF 7  CAPLUS  COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER:         2004:550745  CAPLUS
DOCUMENT NUMBER:          141:106475
TITLE:                    Preparation of 5-membered heterocycle derivatives for
                          treating neurodegenerative disorders or pain
INVENTOR(S):              Chabrier De Lassauniere, Pierre-Etienne; Harnett,
                          Jeremiah; Bigg, Dennis; Liberatore, Anne-Marie;
                          Pommier, Jacques; Lannoy, Jacques; Thurieau,
                          Christophe
```

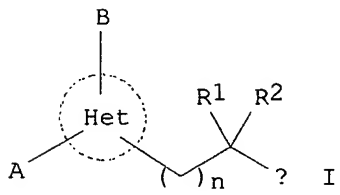
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 150 pp., Cont.-in-part of U.S. Ser. No. 89,993.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004132788	A1	20040708	US 2003-681002	20031008
FR 2799461	A1	20010413	FR 1999-12643	19991011
FR 2799461	B1	20020104		
FR 2812546	A1	20020208	FR 2000-10151	20000801
WO 2001026656	A2	20010419	WO 2000-FR2805	20001010
WO 2001026656	A3	20020418		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1228760	A2	20020807	EP 2002-76763	20001010
EP 1228760	A3	20040128		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				

PRIORITY APPLN. INFO.:

FR 1999-12643	A	19991011
FR 2000-10151	A	20000801
FR 2000-11169	A	20000901
WO 2000-FR2805	W	20001010
JP 1989-4943	A	20010410
JP 1990-1811	A	20020214
US 2002-89993	A2	20020404
EP 2000-967988	A3	20001010

OTHER SOURCE(S): MARPAT 141:106475
GI



AB The invention relates to thiazole, oxazole, imidazole, isoxazole and isoxazoline derivs. of general formula (I) [wherein Het = thiazole, oxazole, imidazole, isoxazole or isoxazoline; n = an integer from 0 to 6; A = optionally substituted aromatic radical; B = H, alkyl, Ph; R1, R2 = H, alkyl, cycloalkyl; Ω = NR46R47 or OR48; R46, R47 = H, alkyl, cycloalkyl, (CH2)k-CO2R51; R51 = alkyl, haloalkyl; R48 = H, alkyl]. These compds. have advantageous pharmacol. properties which allow their use in a medicament intended to inhibit monoamine oxidases (MAO) and/or lipidic peroxidn. and/or to act as modulators of the sodium channels and notably their use in therapeutics for treating (1) central or peripheral nervous system, (2) neurodegenerative disorders selected from Parkinson's disease,

Alzheimer's disease, **Huntington's chorea** and amyotrophic lateral sclerosis or (3) pain selected from the group consisting of postoperative pain, migraine, neuropathic pain, central pain, chronic inflammatory pain and pain linked to a cancer. Thus, 2-[[[(1,1-dimethylethoxy)carbonyl]methyl]amino]ethanethioamide (4.3 g, 2.11 mmol) and 2-bromo-1-(3,5-di-tert-butyl-4-hydroxyphenyl)ethanone (6,9 g, 2,11 mmol) were dissolved in 75 mL benzene under argon atmospheric and stirred at ambient temperature for 12 h to give, after workup and silica gel chromatog., 4-[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]-N-[(1,1-dimethylethoxy)carbonyl]-N-methyl-2-thiazolemethanamine which was treated with CF3CO2H and triethylsilane in 50 mL CH2Cl2 to give, after workup, 4-[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]-N-methyl-2-thiazolemethanamine (II). II showed IC50 of lower than 10 μM for inhibiting lipid peroxidn. of the cerebral cortex of rats.

L16 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2004:467870 CAPLUS
DOCUMENT NUMBER: 141:38625
TITLE: Preparation of Chk-, pdk- and akt-inhibitory pyrimidines
INVENTOR(S): Bryant, Judi; Kochanny, Monica; Yuan, Shendong; Khim, Seock-Kuy; Buckman, Brad; Arnaiz, Damian; Boemer, Ulf; Briem, Hans; Esperling, Peter; Huwe, Peter; Kuhnke, Joachim; Schaefer, Martina; Wortmann, Lars; Kosemund, Dirk; Eckle, Emil; Feldman, Richard; Phillips, Gary
PATENT ASSIGNEE(S): Schering Aktiengesellschaft, Germany
SOURCE: PCT Int. Appl., 293 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004048343	A1	20040610	WO 2003-EP13443	20031128
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004186118	A1	20040923	US 2003-722591	20031128
PRIORITY APPLN. INFO.:			EP 2002-26607 A	20021128
OTHER SOURCE(S):	MARPAT 141:38625			

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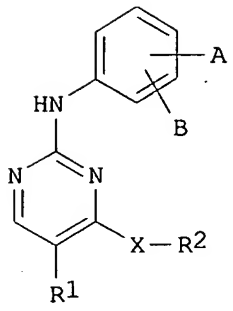

I

AB The title compds. [I; A, B = CN, halo, H, OH, etc.; X = O, (un)substituted NH; R1 = H, halo, CH2OH, alkyl, etc.; R2 = H, (un)substituted NHCO-aryl or alkyl] which are inhibitors of kinases useful as medications for treating various diseases, were prepared E.g., a multi-step synthesis of 5-bromo-4-[2-(1H-imidazol-4-yl)ethylamino]-2-(4-pyrrolidin-1-ylmethylphenylamino)pyrimidine, starting from 5-bromouracil, was given. Biol. data for inhibition of Akt-2, Chk-1, and VEGFR-II (KDR) were given. The pharmaceutical composition comprising the compds. I is claimed.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 3 OF 7 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:319488 CAPLUS
DOCUMENT NUMBER: 138:337988
TITLE: Novel 2-[(iminomethyl)amino]phenyl derivatives useful as inhibitors of NO synthase and lipid peroxidation, their preparation, their application as medicines, and pharmaceutical compositions containing them
INVENTOR(S): Chabrier De Lassauniere, Pierre Etienne; Auvin, Serge; Bigg, Dennis; Auguet, Michel; Harnett, Jeremiah
PATENT ASSIGNEE(S): Societe de Conseils de Recherches et D'Applications scientifiques (S.C.R.A.S.), Fr.
SOURCE: U.S. Pat. Appl. Publ., 78 pp., Cont.-in-part of U.S. Ser. No. 882,264.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003078420	A1	20030424	US 2002-191950	20020709
US 6809088	B2	20041026		
FR 2761066	A1	19980925	FR 1997-3528	19970324
FR 2761066	B1	20001124		
FR 2764889	A1	19981224	FR 1997-7701	19970620
FR 2764889	B1	20000901		
WO 9842696	A1	19981001	WO 1998-FR288	19980216
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WO 9858934	A1	19981230	WO 1998-FR1250	19980615

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
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US 6335445	B1	20020101	US 1999-456205	19991207
US 2002007062	A1	20020117	US 2001-882264	20010615
US 6630461	B2	20031007		

PRIORITY APPLN. INFO.:	FR 1997-3528	A 19970324
	FR 1997-7701	A 19970620
	WO 1998-FR288	W 19980216
	WO 1998-FR1250	W 19980615
	US 1999-456205	A3 19991207
	US 2001-882264	A2 20010615
	US 1999-381749	A2 19990922

OTHER SOURCE(S): MARPAT 138:337988

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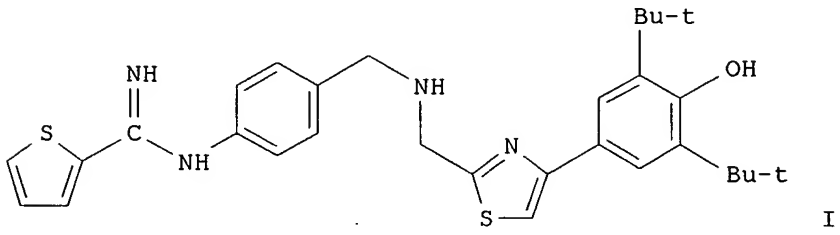

I

AB Title compds., e.g., N-[4-[[[[4-(3,5-di-tert-butyl-4-hydroxyphenyl)-**1,3-thiazol**-2-yl]methyl]amino]methyl]phenyl]th iophene-2-carboximidamide (I) are prepared The compds. are inhibitors of NO synthases, and are also antioxidants which inhibit lipid peroxidn. Approx. 70 examples are prepared I had IC50 for inhibiting rat neuronal NO synthase in vitro < 3.5 μM, and the IC50 for inhibiting rat cerebral lipid peroxidn. in vitro is < 30 μM.

L16 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:	2002:814116 CAPLUS
DOCUMENT NUMBER:	137:325417
TITLE:	Preparation and application of 5-membered heterocycles as medicaments
INVENTOR(S):	Harnett, Jeremiah; Bigg, Dennis; Liberatore, Anne-Marie; Rolland, Alain
PATENT ASSIGNEE(S):	Societe De Conseils De Recherches Et D'applications Scientifiques (SCRAS), Fr.
SOURCE:	PCT Int. Appl., 132 pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	French
FAMILY ACC. NUM. COUNT:	1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002083656	A2	20021024	WO 2002-FR1218	20020409
WO 2002083656	A3	20030103		

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GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

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FR 2823208	B1	20040319			
CA 2443403	AA	20021024	CA 2002-2443403		20020409
EP 1379514	A2	20040114	EP 2002-761921		20020409
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NO 2003004524	A	20031029	NO 2003-4524		20031009
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			WO 2002-FR1218	W	20020409

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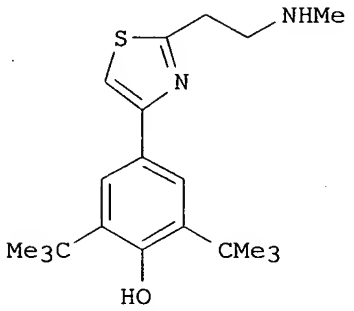

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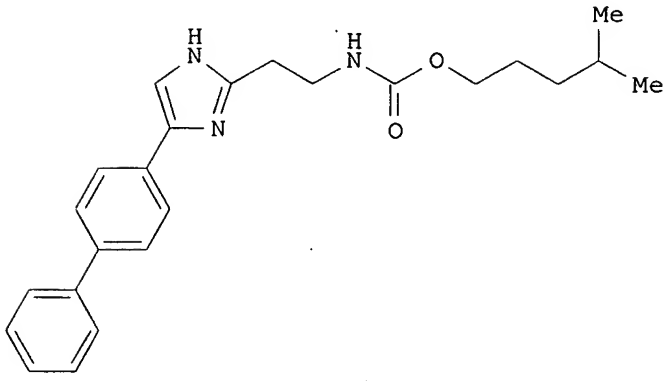

II

AB The invention relates to thiazole, oxazole or imidazole derivs. having at least one of the following pharmacol. activities:: inhibition of monoamine oxydases (MAO); inhibition of lipid peroxidn.; modulation of sodium channels. The inventive compds. comprise, for example, 2,6-di(tert-butyl)-4-{2-[2-(methylamino)ethyl]-**1,3-thiazol**-4-yl}phenol (I); and 4-methylpentyl 2-[4-(1,1'-biphenyl-4-yl)-1H-imidazol-2-yl]ethyl carbamate (II). Thus, I·HCl was prepared from N-methyl-β-alaninenitrile via. N-protection with (Boc)2O in CH2Cl2 containing EtN(CHMe2)2, sulfurization with H2S in EtOH containing Et3N, cyclocondensation with α-bromo-1-[3,5-di(tert-butyl)-4-hydroxyphenyl]ethanone and acid-catalyzed deprotection with HCl in EtOAc.

By virtue of their pharmacol. properties, said compds. can be used to treat one of the following disorders or diseases: Parkinson's disease, senile dementia, Alzheimer's disease, **Huntington**'s **chorea**, amyotrophic lateral sclerosis, schizophrenia, depression, psychoses, migraine or pain, especially neuropathic pain. The pharmacol. activity of I was determined [CI50 ≤ 10 μM vs. monoamine oxydase B; CI50 ≤ 10 μM vs. lipid peroxidn.; CI50 ≤ 1.0 μM on sodium channels from the cerebral cortex of rats].

L16 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:777933 CAPLUS
DOCUMENT NUMBER: 137:294969
TITLE: 4-Aryl-substituted 2-pyrimidinamines and 2-pyridinamines, useful as inhibitors of c-Jun N-terminal kinases (JNK) and other protein kinases
INVENTOR(S): Bethiel, Randy; Cochran, John; Moon, Young-Choon; Nanthakumar, Susanthini
PATENT ASSIGNEE(S): Vertex Pharmaceuticals Incorporated, USA
SOURCE: PCT Int. Appl., 115 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002079197	A1	20021010	WO 2002-US9554	20020328
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
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CA 2441733	AA	20021010	CA 2002-2441733	20020328
US 2003087922	A1	20030508	US 2002-109070	20020328
EP 1373257	A1	20040102	EP 2002-725391	20020328
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JP 2004529140	T2	20040924	JP 2002-577822	20020328

PRIORITY APPLN. INFO.: US 2001-279961P P 20010329
WO 2002-US9554 W 20020328

OTHER SOURCE(S): MARPAT 137:294969
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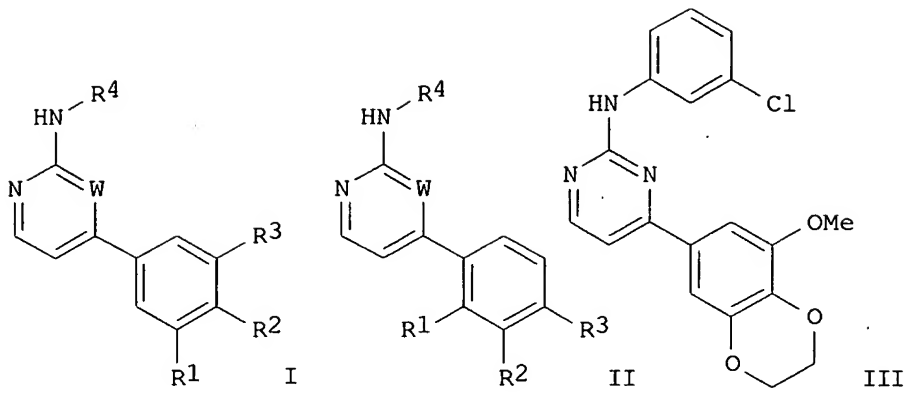

AB The invention provides compds. of formula I and II, and their pharmaceutically acceptable derivs.[wherein: W = N, CH; R1, R2, R3 = halo, QR, QnCN, QnNO2, QnAr2; or R1R2, R2R3 = 4- to 8-membered (un)saturated ring with 0-3 N/O/S atoms; n = 0 or 1; Q = C1-4 alkylidene with one CH2 optionally replaced by O, S, NR, NRCO, CO, CO2, CONR, SO2, SO2NR, NRSO2NR, etc.; R = H, (un)substituted aliphatic; or NRR = 3- to 7-membered (un)saturated ring with 1-2 addnl. N/O/S atoms; R4 = Ar1, TAr2, TnAr3; T = C1-2 alkylidene with optional replacement of a CH2 as above; Ar1 = (un)substituted 5- to 6-membered mono- or bicyclic (un)saturated ring system; Ar2 = (un)substituted 5- to 6-membered (un)saturated monocyclic ring with 0-3 N/O/S atoms, or (un)substituted 8- to 10-membered (un)saturated bicyclic ring with 0-5 N/O/S atoms; Ar3 = 6-membered aryl with 0-2 N atoms and substituted with certain groups; with provisos and exclusions]. The compds. are inhibitors of protein kinases, particularly JNK, a mammalian protein kinase involved in cell proliferation, cell death and response to extracellular stimuli. Furthermore, they are inhibitors of Src-family kinases, especially Src and Lck kinases. The compds. are also inhibitors of GSK3 and CDK2 kinases. The invention also relates to methods for producing the compds. Also provided are pharmaceutical compns. comprising I or II, and methods of utilizing those compns. in the treatment and prevention of various disorders. Three tables of approx. 240 compds. were prepared and claimed., and most were tested against at least one of the five mentioned kinases. For instance, 3,4-dihydroxy-5-methoxybenzaldehyde was cyclized with 1,2-dibromoethane to give a benzodioxane derivative, followed by elaboration of the formyl group to Me2NCH:CH:CO- in 3 steps. Cyclization of the resultant enaminone with 3-chlorophenylguanidine gave title compound III. This compound inhibited cloned human JNK3 protein in vitro with Ki < 0.1 μM.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 6 OF 7 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2002:107318 CAPLUS
DOCUMENT NUMBER: 136:151163
TITLE: Preparation of indazole derivatives as JNK enzyme inhibitors
INVENTOR(S): Bhagwat, Shripad S.; Satoh, Yoshitaka; Sakata, Steven T.
PATENT ASSIGNEE(S): Signal Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 412 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002010137	A2	20020207	WO 2001-US23890	20010730
WO 2002010137	C2	20030206		
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CA 2417650	AA	20020207	CA 2001-2417650	20010730
EP 1313711	A2	20030528	EP 2001-957332	20010730
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JP 2004513882	T2	20040513	JP 2002-516269	20010730
NZ 524045	A	20040730	NZ 2001-524045	20010730
PRIORITY APPLN. INFO.:			US 2000-221799P	P 20000731
			WO 2001-US23890	W 20010730

OTHER SOURCE(S): MARPAT 136:151163

AB Indazole derivs., 3-R1A-5-R2-1H-indazoles (1), having activity as selective inhibitors of JNK are disclosed. In 1: A is a direct bond, -(CH2)a-, -(CH2)bCH:CH(CH2)c-, or -(CH2)bC.tplbond.C(CH2)c-; R1 is aryl, heteroaryl or heterocycle fused to Ph, each being optionally substituted with 1-4 R3; R2 is -R3, -R4, -(CH2)bC(O)R5, -(CH2)bC(:O)OR5, -(CH2)bC(O)NR5R6, -(CH2)bC(O)NR5(CH2)cC(O)R6, -(CH2)bNR5C(O)R6, -(CH2)bNR5C(O)NR6R7, -(CH2)bNR5R6, -(CH2)bOR5, -(CH2)bSOdR5 or -(CH2)bSO2NR5R6. A is 1-6; b and c are the same or different and are 0-4; d is 0-2. R3 is at each occurrence independently halogen, hydroxy, carboxy, alkyl, alkoxy, haloalkyl, acyloxy, thioalkyl, sulfinylalkyl, sulfonylalkyl, hydroxyalkyl, aryl, substituted aryl, arylalkyl, substituted arylalkyl, heterocycle, substituted heterocycle, heterocyclealkyl, substituted heterocyclealkyl, -C(O)OR8, -C(O)R8, -C(O)NR8R9, -C(O)NR8OR9, -SO2NR8R9, -NR8SO2R9, -CN, -NO2, -NR8R9, -NR8C(O)R9, -NR8C(O)(CH2)bOR9, -NR8C(O)(CH2)bR9, -O(CH2)bNR5R9, or heterocycle fused to Ph. R4 is alkyl, aryl, arylalkyl, heterocycle or heterocyclealkyl, each being optionally substituted with 1-4 R3, or R4 is halogen or hydroxy. R5, R6and R7 are the same or different and are H, alkyl, aryl, arylalkyl, heterocycle or heterocyclealkyl, wherein each of R5, R6 and R7 are optionally substituted with 1-4 R3. R8 and R9 are the same or different and at each occurrence independently H, alkyl, aryl, arylalkyl, heterocycle, or heterocyclealkyl, or R8 and R9 taken together with the atom or atoms to which they are bonded form a heterocycle, wherein each of R8, R9, and R8 and R9 taken together to form a heterocycle are optionally substituted with 1-4 R3 with the proviso that: when A is a direct bond and R1 is Ph, R2 is not Me, methoxy, C(O)CH3 or C(O)H; when A is a direct bond and R1 is 4-Me-Ph, R2 is not Me; when A is a direct bond and R1 is 4-F-Ph, R2 is not trifluoromethyl; when A is a direct bond or -C.tplbond.C- and R1 is Ph, R2 is not -COOEt; and when A is a direct bond and R1 is 6,7-dimethoxyisoquinolin-1-yl, R2 is not hydroxy. Such compds. have utility in the treatment of a wide range of conditions that are responsive to JNK inhibition. Thus, methods of treating such conditions are also disclosed, as are pharmaceutical compns. containing one or more compds. of the above compds. Many of the claimed compds. have IC50 values ≤0.5 μM in the JNK2 assay, e.g. 5-[3-(4-fluorophenyl)-1H-indazol-5-yl]-2H-1,2,3,4-tetrazole. Although the methods of preparation are not claimed, >400 example prepns. are included.

L16 ANSWER 7 OF 7 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:283789 CAPLUS

DOCUMENT NUMBER: 134:311210
TITLE: 5-Membered heterocycle derivatives useful as monoamine oxidase inhibitors, lipid peroxidation inhibitors, and sodium channel modulators, and the production thereof, and use thereof as medicaments
INVENTOR(S): Chabrier de Lassauniere, Pierre-Etienne; Harnett, Jeremiah; Bigg, Dennis; Pommier, Jacques; Lannoy, Jacques; Liberatore, Anne-Marie; Thurieau, Christophe
PATENT ASSIGNEE(S): Societe de Conseils de Recherches et d'Applications Scientifiques (S.C.R.A.S, Fr.
SOURCE: PCT Int. Appl., 261 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001026656	A2	20010419	WO 2000-FR2805	20001010
WO 2001026656	A3	20020418		
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FR 2799461	B1	20020104		
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CA 2388505	AA	20010419	CA 2000-2388505	20001010
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EP 1223933	A2	20020724	EP 2000-967988	20001010
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NO 2002001689	A	20020530	NO 2002-1689	20020410
US 2004132788	A1	20040708	US 2003-681002	20031008

PRIORITY APPLN. INFO.:

FR 1999-12643	A	19991011
FR 2000-10151	A	20000801
FR 2000-11169	A	20000901
EP 2000-967988	A3	20001010
EP 2002-76763	A3	20001010
WO 2000-FR2805	W	20001010
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US 2002-89993	A2	20020404

OTHER SOURCE(S): MARPAT 134:311210
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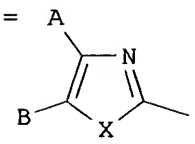
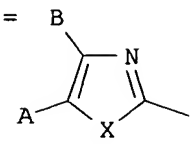
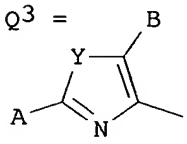
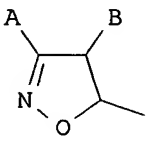
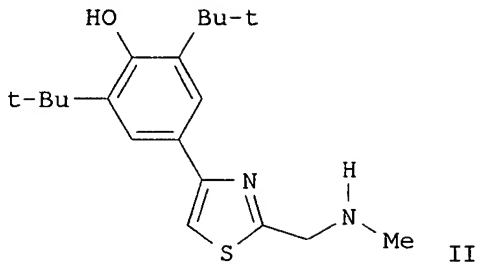
Q1 = 

Q2 = 

Q3 = 

Q4 = 



II

AB The invention relates to pharmaceutical use of heterocyclic compds. of general formula Het(A)(B)-(CH2)n-CR1R2-Q [I; wherein the substituted heterocyclic ring Het(A)(B) = Q1-Q4; A = various aryl or heteroaryl systems, especially a substituted Ph or biphenyl radical, or also alkyl, cycloalkyl, or cycloalkylalkyl; B = especially H or alkyl, or also aryl or substituted alkyl; X = especially NH or S, or also substituted NH; Y = O or S; n = 0-6; R1, R2 = especially H, alkyl, or cycloalkyl; Q = NR3R4 or OR5; R3 and R4 = especially H, alkyl, cycloalkyl, alkynyl, cyanoalkyl alkoxycarbonyl, aralkoxycarbonyl or (cycloalkyl)oxycarbonyl; R5 = H, alkyl, alkynyl, or cyanoalkyl]. I and their racemates, enantiomers, and/or salts can be used for producing medicaments for inhibiting monoamine oxidases (MAO), inhibiting lipid peroxidn., and/or for acting as modulators of sodium channels. The resulting medicaments are particularly for use in treating Parkinson's disease, senile dementia, Alzheimer's disease, **Huntington**'s **chorea**, amyotrophic lateral sclerosis, schizophrenia, depression, psychosis, pain and epilepsy. Approx. 350 synthetic examples of I and their salts are given, and numerous free bases of I are claimed. For instance, protection of sarcosinamide-HCl with BOC anhydride gave 72% BOC-N(Me)CH2CONH2, which was converted to the thioamide with (P2S5)2 in 65% yield. Cyclocondensation of the thioamide with 2-bromo-1-(3,5-di-tert-butyl-4-hydroxyphenyl)ethanone (28%), followed by deprotection (73%) and salification (92%), gave thiazole derivative II as the HCl salt. II inhibited binding of the MAO-B specific ligand [3H]-Ro-19-6327 to rat mitochondrial prepns. with IC50 < 10 μM. Selected I also inhibited formation of malondialdehyde by lipid peroxidn. in rat cerebral cortex prepns., and inhibited specific binding of [3H]-batrachotoxin to voltage-dependent sodium channels in rat cerebral cortex homogenates.

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MISMATCHED QUOTE 'PARKINSON'S'
Quotation marks (or apostrophes) must be used in pairs,
one before and one after the expression you are setting

off or masking.

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        726603 DISEASE
        200824 DISEASES
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L20             1 (L18 OR L19) AND L17

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L20  ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER:         2002:171898  CAPLUS
DOCUMENT NUMBER:          136:232298
TITLE:                    Pyrazolopyridine compounds and pharmaceutical use
                          thereof as adenosine receptor antagonists
INVENTOR(S):              Akahane, Atsushi; Tanaka, Akira; Minagawa, Masatoshi;
                          Itani, Hiromichi; Ohtake, Hiroaki
PATENT ASSIGNEE(S):       Fujisawa Pharmaceutical Co., Ltd., Japan
SOURCE:                   PCT Int. Appl., 149 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.          DATE
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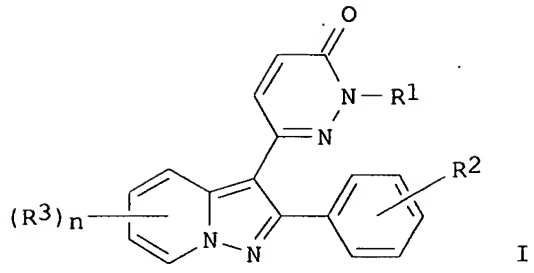

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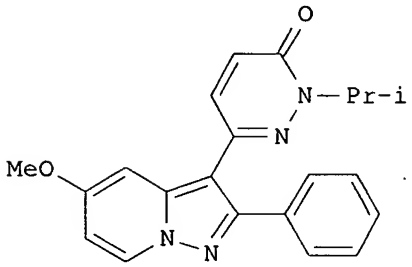

II

AB Pyrazolopyridines I are disclosed [wherein: R1 = H, (un)substituted lower alkyl or cycloalkyl which may be interrupted by an O or N; R2 = H, halo, or lower alkoxy; R3 = independent substituent(s); and n = 1 to 4; or a salt thereof]. The compds. are adenosine antagonists, and are thus useful for the prevention and/or treatment of a wide variety of medical conditions, e.g., depression, dementia (e.g., Alzheimer's disease, cerebrovascular dementia, dementia accompanying Parkinson's disease, etc.) Parkinson's disease, anxiety, pain, cerebrovascular disease (e.g. stroke, etc.), heart failure, and the like. In particular, treatment of Parkinson's disease and/or associated symptoms is specifically claimed. Over 330 example compds. are described. For instance, cyclization of 1-amino-4-methoxypyridinium iodide with 3-(benzenesulfonyl)-6-(phenylethynyl)pyridazine, gave 3-(3-phenylsulfonylpyridazin-6-yl)-5-methoxy-2-phenylpyrazolo[1,5-a]pyridine. This compound was hydrolyzed at the phenylsulfinyl group, and the resultant pyridazinone was N-alkylated with NaH/DMF and iso-PrI to give title compound II. In radioligand binding assays, II had Ki values of 0.15 nM for human A1 receptors and 1.38 nM for human A2A receptors. In an anticatalepsy test in mice, 6 tested example compds. I at 3.2 mg/kg orally completely suppressed the cataleptic effects of haloperidol at 0.32 mg/kg i.p.

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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=> s (Alzheimer?(w)disease or anit-alzheimer?(w)agents)
        32570 ALZHEIMER?
       726603 DISEASE
       200824 DISEASES
       820377 DISEASE
                (DISEASE OR DISEASES)
        12898 ALZHEIMER?(W)DISEASE
          242 ANIT
           30 ANITS
          272 ANIT
                (ANIT OR ANITS)
        32570 ALZHEIMER?
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                (ANIT(W)ALZHEIMER?)
       1004755 AGENTS
             0 ANIT-ALZHEIMER?(W)AGENTS
L21      12898 (ALZHEIMER?(W)DISEASE OR ANIT-ALZHEIMER?(W)AGENTS)

=> s L12 and L21
L22        134 S L12
L23         39 S L12
L24          2 (L22 OR L23) AND L21

=> d L24 ibib abs 1-2

L24  ANSWER 1 OF 2  CAPLUS  COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER:         2003:696859  CAPLUS
DOCUMENT NUMBER:          139:230480
TITLE:                    Preparation of substituted amines prodrugs useful in
                          treating Alzheimer's disease
INVENTOR(S):              Varghese, John; Jagodzinska, Barbara; Maillard,
                          Michel; Beck, James P.; Tenbrink, Ruth E.; Getman,
                          Daniel
PATENT ASSIGNEE(S):       Elan Pharmaceuticals, Inc., USA; Pharmacia & Upjohn
SOURCE:                   PCT Int. Appl., 483 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.         DATE
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     WO 2003072535         A2    20030904    WO 2003-US7287          20030227
     WO 2003072535         C1    20040930
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
             PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ,
             UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
             KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
             FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF,
             BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.:                        US 2002-359953P     P  20020227
OTHER SOURCE(S):          MARPAT 139:230480
GI
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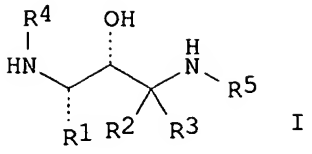

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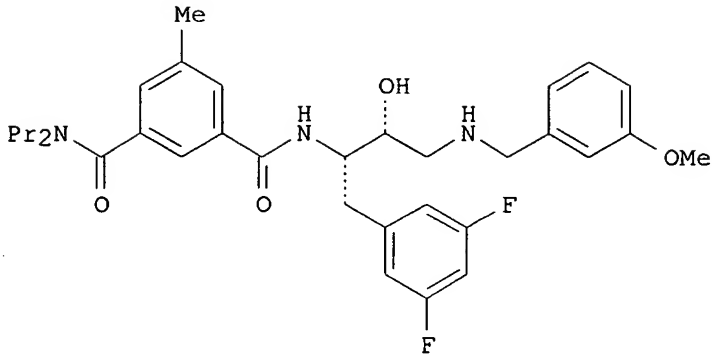

II

AB Amines [I; R1 = (un)substituted alkyl, alkenyl, alkynyl, etc.; R2 = H, (un)substituted alkyl, alkenyl, etc.; R3 = H, (un)substituted alkyl, alkenyl, etc.; R4 = XR; X = CO, SO2, a bond, etc.; R = Ph, naphthyl, indanyl, etc.; R5 = (un)substituted alkyl, (CH2)0-3cycloalkyl, etc.; e.g. N1-[(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]-5-methyl-N3,N3-dipropylisophthalamide], useful in treating Alzheimer's disease and other similar diseases, were prepared Although the methods of preparation are not claimed, hundreds of example prepns. are included. Thus, reacting (2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(3-methoxybenzyl)amino]-2-butanol trifluoroacetate with 5-methyl-N,N-dipropylisophthalamic acid in the presence of Et3N, 1-hydroxybenzotriazole and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride in DMF afforded (1S,2R)-II (N1-[(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]-5-methyl-N3,N3-dipropylisophthalamide). The compds. I exhibit an IC50 of < 50 μM against β-secretase.

L24 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:	2001:137023 CAPLUS
DOCUMENT NUMBER:	134:178552
TITLE:	3(5)-Acylaminopyrazole derivatives, process for their preparation and their use as antitumor agents
INVENTOR(S):	Pevarello, Paolo; Orsini, Paolo; Traquandi, Gabriella; Varasi, Mario; Fritzen, Edward L.; Warpehoski, Martha A.; Pierce, Betsy S.; Brasca, Maria Grabriella
PATENT ASSIGNEE(S):	Pharmacia & Upjohn S.p.A., Italy; Pharmacia & Upjohn Company
SOURCE:	PCT Int. Appl., 123 pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	1
PATENT INFORMATION:	

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001012189	A1	20010222	WO 2000-US6699	20000505

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG,

MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
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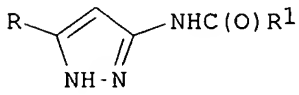
CA 2383555	AA	20010222	CA 2000-2383555		20000505
AU 2000049714	A5	20010313	AU 2000-49714		20000505
EP 1202733	A1	20020508	EP 2000-931906		20000505
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL					
BR 2000013143	A	20020611	BR 2000-13143		20000505
JP 2003507329	T2	20030225	JP 2001-516535		20000505
EE 200200065	A	20030415	EE 2002-65		20000505
NZ 517237	A	20040227	NZ 2000-517237		20000505
US 6218418	B1	20010417	US 2000-667603		20000922
NO 2002000684	A	20020403	NO 2002-684		20020211
HR 2002000128	A1	20030430	HR 2002-128		20020212
ZA 2002001511	A	20030311	ZA 2002-1511		20020222
BG 106480	A	20020930	BG 2002-106480		20020305
PRIORITY APPLN. INFO.:			US 1999-372831	A	19990812
			US 2000-560400	A1	20000428
			WO 2000-US6699	W	20000505

OTHER SOURCE(S): MARPAT 134:178552
GI



I

AB Compds. which are 3-acylaminopyrazole derivs. (I; e.g. N-(5-cyclopropyl-1H-pyrazol-3-yl)-2,2-diphenylacetamide) wherein R is C3-C6 cycloalkyl group optionally substituted by a straight or branched C1-C6 alkyl or arylalkyl group; R1 is a straight or branched C1-C6 alkyl, C2-C4 alkenyl, cycloalkyl, cycloalkenyl, heterocyclyl, aryl, arylalkyl, arylcarbonyl, aryloxyalkyl or arylalkenyl group, each of which may be optionally further substituted as indicated in the description; or a pharmaceutically acceptable salt thereof, processes for their preparation and their therapeutic uses. The compds. are useful for the treatment of cancer, cell proliferative disorders, Alzheimer's disease, viral infections, auto-immune diseases or neurodegenerative diseases, but no quant. test results are presented. The cancer is selected from carcinoma, squamous cell carcinoma, hematopoietic tumors of myeloid or lymphoid lineage, tumors of mesenchymal origin, tumors of the central and peripheral nervous system, melanoma, seminoma, teratocarcinoma, osteosarcoma, xeroderma pigmentosum, keratoacanthoma, thyroid follicular cancer and Kaposi's sarcoma. The cell proliferative disorder is selected from benign prostate hyperplasia, familial adenomatosis polyposis, neuro-fibromatosis, psoriasis, vascular smooth cell proliferation associated with atherosclerosis, pulmonary fibrosis, arthritis glomerulonephritis and post-surgical stenosis and restenosis. The method of treatment provides tumor angiogenesis and metastasis inhibition, cell cycle inhibition or cdk/cyclin dependent inhibition, and treatment or prevention of radiotherapy-induced or chemotherapy-induced alopecia. A process for preparing the 3-aminopyrazole derivative or the pharmaceutically acceptable salt thereof, comprising: (a) reacting RCO2R2 (R2 = alkyl), with MeCN in the presence of a basic agent, to obtain RC(O)CH2CN; (b) reacting RC(O)CH2CN with hydrazine hydrate to obtain an 3-amino-5-R-1H-pyrazole; (c) oxidizing the 3-amino-5-R-1H-pyrazole to obtain the nitro analog; (d) reacting the

nitro compound with tert-butoxycarbonyl anhydride (Boc2O) to obtain the N-Boc derivative; (e) reducing this BOC derivative to obtain the amino analog;
(f)
reacting this amino compound with R1C(O)X (X = OH or a suitable leaving group) to obtain the N1-Boc-protected I; and (g) hydrolyzing this intermediate in an acidic medium to obtain I. Other methods of preparation are also claimed.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

```
=> s schizophrenia?
L25      12467 SCHIZOPHRENIA?

=> s L12 and L25
L26        134 S L12
L27         39 S L12
L28         21 (L26 OR L27) AND L25

=> d L28 ibib all 1-21
```

L28 ANSWER 1 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2004:822842 CAPLUS
DOCUMENT NUMBER: 141:314346
TITLE: Preparation of quinoline, tetrahydroquinazoline, and pyrimidine derivatives as MCH antagonist for treatment of CNS disorders
INVENTOR(S): Sekiguchi, Yoshinori; Kanuma, Kosuke; Omodera, Katsunori; Busujima, Tsuyoshi; Tran, Thuy-Anh; Han, Sangdon; Casper, Martin; Kramer, Bryan A.; Semple, Graeme; Zou, Ning
PATENT ASSIGNEE(S): Taisho Pharmaceutical Co. Ltd., Japan; Arena Pharmaceuticals, Inc.
SOURCE: Eur. Pat. Appl., 586 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1464335	A2	20041006	EP 2004-7651	20040330
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK				
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WO 2004087669	A1	20041014	WO 2004-JP4624	20040331
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JP 2004300156	A2	20041028	JP 2004-107965		20040331
PRIORITY APPLN. INFO.:			US 2003-458530P	P	20030331
			US 2003-495911P	P	20030819
			US 2003-510186P	P	20031009
			US 2003-530360P	P	20031216
			EP 2004-7651	A	20040330

OTHER SOURCE(S): MARPAT 141:314346

AN 2004:822842 CAPLUS

DN 141:314346

ED Entered STN: 08 Oct 2004

TI Preparation of quinoline, tetrahydroquinazoline, and pyrimidine derivatives as MCH antagonist for treatment of CNS disorders

IN Sekiguchi, Yoshinori; Kanuma, Kosuke; Omodera, Katsunori; Busujima, Tsuyoshi; Tran, Thuy-Anh; Han, Sangdon; Casper, Martin; Kramer, Bryan A.; Semple, Graeme; Zou, Ning

PA Taisho Pharmaceutical Co. Ltd., Japan; Arena Pharmaceuticals, Inc.

SO Eur. Pat. Appl., 586 pp.
CODEN: EPXXDW

DT Patent

LA English

IC ICM A61K031-4709
ICS C07D401-12; C07D403-12; C07D405-12; C07D409-12; C07D413-12; C07D417-12; C07D417-14; C07D215-38; A61K031-506; A61P003-04

CC 28-16 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 63

FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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	EP 1464335	A2	20041006	EP 2004-7651	20040330
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK				
	EP 1464335	A2	20041006	EP 2004-7651	20040330
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK				
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	US 2003-495911P	P	20030819		
	US 2003-510186P	P	20031009		
	US 2003-530360P	P	20031216		
	EP 2004-7651	A	20040330		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
EP 1464335	ICM	A61K031-4709
	ICS	C07D401-12; C07D403-12; C07D405-12; C07D409-12; C07D413-12; C07D417-12; C07D417-14; C07D215-38; A61K031-506; A61P003-04
JP 2004300156	FTERM	4C031/LA01; 4C063/AA01; 4C063/AA03; 4C063/BB09;

4C063/CC29; 4C063/CC31; 4C063/CC58; 4C063/CC75;
4C063/CC79; 4C063/CC81; 4C063/CC92; 4C063/DD02;
4C063/DD04; 4C063/DD06; 4C063/DD07; 4C063/DD12;
4C063/DD14; 4C063/DD22; 4C063/DD29; 4C063/DD31;
4C063/EE01; 4C086/AA01; 4C086/AA02; 4C086/AA03;
4C086/AA04; 4C086/BC28; 4C086/BC42; 4C086/BC46;
4C086/BC71; 4C086/BC82; 4C086/BC84; 4C086/GA02;
4C086/GA04; 4C086/GA07; 4C086/GA08; 4C086/GA09;
4C086/GA10; 4C086/MA01; 4C086/MA04; 4C086/ZA02;
4C086/ZA06; 4C086/ZA12; 4C086/ZA15; 4C086/ZA18;
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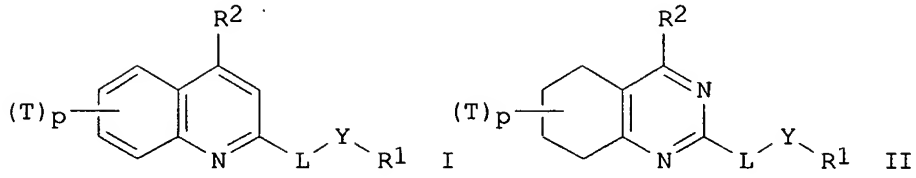
4C086/ZC33; 4C086/ZC35

OS MARPAT 141:314346

GI



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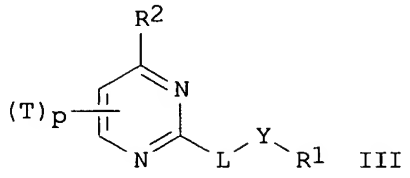

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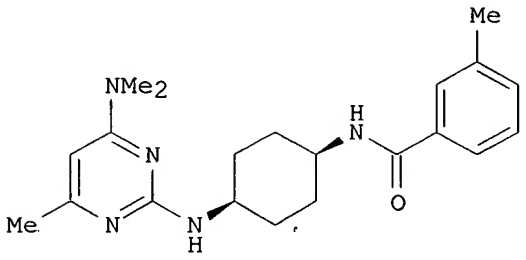


IV

AB Title compds. I, II, and III [wherein R1 = (un)substituted (cyclo)alkyl, (cyclo)alkenyl, alkynyl, aryl; R2 = H, halo, OH, carboxy, carbamoyl, amino, (un)substituted alkyl, alkoxy; T = independently H, halo, OH, carboxy, carbamoyl, amino, cyano, NO2, alkenyl, alkynyl, cycloalkyl, (un)substituted alkyl, alkoxy; p = 0-5; L = aminocycloalkylideneamino, etc.; Y = bond, CH2, CO2, OCO, SO2, CO, CS, CONH, CSNH, etc.; with provisos; and pharmaceutically acceptable salts, hydrates, or solvates thereof] were prepared as antagonists of melanin concentrating hormone (MCH), an endogenous ligand of G-protein coupled receptors (GPCRs). Examples include solution and solid phase general synthetic methods and phys. data for nearly 3400 invention compds. In addition, all exemplified compds. were assayed using high throughput functional screening to detect intracellular Ca2+ concns. for accessing GPCR activation. For instance, reaction of 2,4-dichloro-6-methylpyrimidine with dimethylamine gave 2-chloro-4-(dimethylamino)-6-methylpyrimidine (40%), which was coupled with cis-(4-aminocyclohexyl)carbamic acid tert-Bu ester (60%).

Deprotection (72%), amidation, and workup provided the benzamide IV•TFA. The latter demonstrated MCH antagonist activity with an IC50 value of 7.6 nM. Thus, pharmaceutical compns. comprising I are useful for the prophylaxis or treatment of improving memory function, sleeping and arousal, anxiety, depression, mood disorders, seizure, obesity, diabetes, appetite and eating disorders, cardiovascular disease, hypertension, dyslipidemia, myocardial infarction, binge eating disorders including bulimia, anorexia, mental disorders including manic depression, **schizophrenia**, delirium, dementia, stress, cognitive disorders, attention deficit disorder, substance abuse disorders, and dyskinesias including Parkinson's disease, epilepsy, and addiction (no data). This is part I of three in a series covering the patent.

ST quinoline quinazoline pyrimidine prepn melanin concg hormone antagonist; pyrimidine quinazoline quinoline prepn MCH antagonist CNS drug

IT Drugs of abuse
(abuse of; preparation of quinolines, quinazolines, and pyrimidines as MCH antagonist for treatment of CNS disorders)

IT Behavior
(arousal; preparation of quinolines, quinazolines, and pyrimidines as MCH antagonist for treatment of CNS disorders)

IT Mental disorder
(attention deficit disorder; preparation of quinolines, quinazolines, and pyrimidines as MCH antagonist for treatment of CNS disorders)

IT Mental disorder
(bipolar disorder; preparation of quinolines, quinazolines, and pyrimidines as MCH antagonist for treatment of CNS disorders)

IT Appetite
(bulimia; preparation of quinolines, quinazolines, and pyrimidines as MCH antagonist for treatment of CNS disorders)

IT Nervous system, disease
(central; preparation of quinolines, quinazolines, and pyrimidines as MCH antagonist for treatment of CNS disorders)

IT Mental disorder
(cognitive; preparation of quinolines, quinazolines, and pyrimidines as MCH antagonist for treatment of CNS disorders)

IT Mental disorder
(dementia; preparation of quinolines, quinazolines, and pyrimidines as MCH antagonist for treatment of CNS disorders)

IT Mental disorder
(depression; preparation of quinolines, quinazolines, and pyrimidines as MCH antagonist for treatment of CNS disorders)

IT Appetite
Cognition
Memory, biological
(disorder; preparation of quinolines, quinazolines, and pyrimidines as MCH antagonist for treatment of CNS disorders)

IT Nervous system, disease
(dyskinesia; preparation of quinolines, quinazolines, and pyrimidines as MCH antagonist for treatment of CNS disorders)

IT Lipids, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(dyslipidemia; preparation of quinolines, quinazolines, and pyrimidines as MCH antagonist for treatment of CNS disorders)

IT Heart, disease
(infarction; preparation of quinolines, quinazolines, and pyrimidines as MCH antagonist for treatment of CNS disorders)

IT Mental disorder
(mood-affecting; preparation of quinolines, quinazolines, and pyrimidines as MCH antagonist for treatment of CNS disorders)

IT Anorexia
Anticonvulsants
Antidepressants
Antidiabetic agents

ylamino)cyclohexyl]methyl]carbamic acid benzyl ester 769175-46-4P, 2-[(cis-4-Aminocyclohexyl)amino]-4-(dimethylamino)quinoline 769175-50-0P, 2-[(cis-4-Aminomethylcyclohexyl)amino]-4-(dimethylamino)quinoline 769175-53-3P, 2-[(cis-4-Aminocyclohexyl)amino]-4-(methylamino)-5,6,7,8-tetrahydroquinazoline 769175-56-6P, [[cis-4-(4-Methylamino-5,6,7,8-tetrahydroquinazolin-2-ylamino)cyclohexyl]methyl]carbamic acid benzyl ester 769175-59-9P, 2-[(cis-4-Aminocyclohexyl)amino]-4-(dimethylamino)-5,6,7,8-tetrahydroquinazoline 769175-64-6P, [cis-4-[(4-Bromo-2-trifluoromethoxybenzyl)amino]cyclohexyl]carbamic acid tert-butyl ester 769175-66-8P, [cis-4-(4-Dimethylaminopyrimidin-2-ylamino)cyclohexyl]carbamic acid tert-butyl ester 769175-67-9P, 2-[(cis-4-Aminocyclohexyl)amino]-4-(dimethylamino)pyrimidine 769175-70-4P, 2-[(cis-4-Aminomethylcyclohexyl)amino]-4-(dimethylamino)pyrimidine
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of quinolines, quinazolines, and pyrimidines as MCH antagonist for treatment of CNS disorders)

IT 67382-96-1, Melanin-concentrating hormone
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(preparation of quinolines, quinazolines, and pyrimidines as MCH antagonist for treatment of CNS disorders)

IT 86-95-3, Quinoline-2,4-diol 619-81-8, cis-Cyclohexane-1,4-dicarboxylic acid 1655-07-8, 2-Oxocyclohexanecarboxylic acid ethyl ester 3685-23-2, cis-4-Aminocyclohexanecarboxylic acid 3934-20-1, 2,4-Dichloropyrimidine 175278-12-3, 4-Bromo-1-iodo-2-trifluoromethoxybenzene 769175-44-2, 2-[[cis-4-[[(4-Bromo-2-trifluoromethoxybenzyl)amino]methyl]cyclohexyl]amino]-4-(methylamino)quinoline 769175-71-5, 2-[(cis-4-Aminomethylcyclohexyl)amino]-4-(dimethylamino)-5,6,7,8-tetrahydroquinazoline
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of quinolines, quinazolines, and pyrimidines as MCH antagonist for treatment of CNS disorders)

L28 ANSWER 2 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:533974 CAPLUS
DOCUMENT NUMBER: 141:89087
TITLE: Preparation of 2-(**piperazinylmethyl**)-1H-benzimidazoles and related compounds that are useful in treating sexual dysfunction
INVENTOR(S): Cowart, Marlon D.; Patel, Meena V.; Kolasa, Teodozyi; Brioni, Jorge D.; Rohde, Jeffrey J.; Engstrom, Kenneth M.; Stewart, Andrew O.; Daanen, Jerome F.; Bhatia, Pramila A.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 59 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2004127504	A1	20040701	US 2003-656672		20030905
PRIORITY APPLN. INFO.:			US 2002-408784P	P	20020906

OTHER SOURCE(S): MARPAT 141:89087
AN 2004:533974 CAPLUS
DN 141:89087
ED Entered STN: 02 Jul 2004
TI Preparation of 2-(**piperazinylmethyl**)-1H-benzimidazoles and related compounds that are useful in treating sexual dysfunction

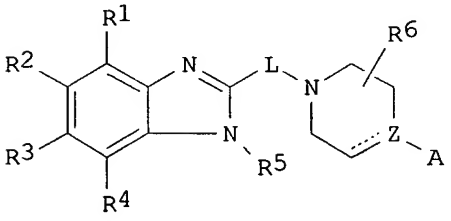
IN Cowart, Marlon D.; Patel, Meena V.; Kolasa, Teodozyi; Brioni, Jorge D.; Rohde, Jeffrey J.; Engstrom, Kenneth M.; Stewart, Andrew O.; Daanen, Jerome F.; Bhatia, Pramila A.
PA USA
SO U.S. Pat. Appl. Publ., 59 pp.
CODEN: USXXCO
DT Patent
LA English
IC ICM A61K031-496
ICS A61K031-4545; A61K031-454
NCL 514253090; 514254060; 514320000; 514318000
CC 28-9 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2004127504	A1	20040701	US 2003-656672	20030905
PRAI US 2002-408784P	P	20020906		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
US 2004127504	ICM	A61K031-496
	ICS	A61K031-4545; A61K031-454
	NCL	514253090; 514254060; 514320000; 514318000
US 2004127504	ECLA	A61K031/454; A61K031/4545; A61K031/496; C07D235/14; C07D401/06; C07D401/12; C07D403/12; C07D417/12

OS MARPAT 141:89087
GI



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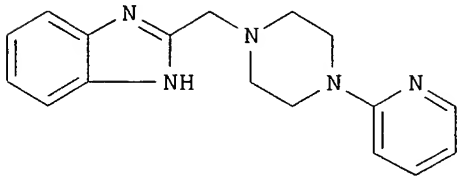


II

AB Title compds. (I) [wherein A = (un)substituted Ph, pyridinyl, pyrimidinyl, thienyl, pyrrolyl, furyl, imidazolyl, pyrazolyl, (is)oxazolyl, (iso)thiazolyl, triazolyl, tetrazolyl, etc.; L = CH2, CH2CH2, CH2CH2CH2, or CH2CH2CH2CH2; R1-R4 = independently H, alkoxy(carbonyl), alkenyl, (halo)alkyl, alkylthio, alkylsulfinyl, alkylsulfonyl, alkynyl, alkylcarbonyl(oxy), CO2H, CN, CHO, halo(alkoxy), OH, hydroxyalkyl, SH, NO2, or (un)substituted amino or carbamoyl; R5 = H, alkoxycarbonyl, alkyl, (cyclo)alkylcarbonyl, arylcarbonyl, heterocyclylcarbonyl, or (un)substituted carbamoyl; R6 = H or alkyl; Z = N, C, or CH; or pharmaceutically acceptable salt, ester, amide, or prodrug thereof] were prepared as dopamine agonists (no data) for the treatment of sexual dysfunction. For example, 2-chloromethylbenzimidazole and TEA were added to 1-(2-pyridyl)**piperazine** in DMF and the solution stirred at 20° for 16 h to give 2-[(4-pyridin-2-**ylpiperazin**

-1-yl)methyl]-1H-benzimidazole (II) in 72% yield. The latter induced penile erection in Wistar rats with an incidence of 83% at a dose of 0.03 μmol/kg without inducing emesis.

ST piperidinylmethyl benzimidazole prepn sexual dysfunction dopamine agonist

IT Drugs of abuse
(abuse of; preparation of (heterocyclylalkyl)benzimidazole dopamine agonists for treatment of sexual dysfunction and other dopamine related disorders)

IT Mental disorder
(attention deficit hyperactivity disorder; preparation of (heterocyclylalkyl)benzimidazole dopamine agonists for treatment of sexual dysfunction and other dopamine related disorders)

IT Adrenoceptor antagonists
Dopamine agonists
(coadministration; preparation of (heterocyclylalkyl)benzimidazole dopamine agonists for treatment of sexual dysfunction and other dopamine related disorders)

IT Mental disorder
(depression; preparation of (heterocyclylalkyl)benzimidazole dopamine agonists for treatment of sexual dysfunction and other dopamine related disorders)

IT Sexual behavior
(disorder, female; preparation of (heterocyclylalkyl)benzimidazole dopamine agonists for treatment of sexual dysfunction and other dopamine related disorders)

IT Sexual behavior
(impotence; preparation of (heterocyclylalkyl)benzimidazole dopamine agonists for treatment of sexual dysfunction and other dopamine related disorders)

IT Mental disorder
(mood-affecting; preparation of (heterocyclylalkyl)benzimidazole dopamine agonists for treatment of sexual dysfunction and other dopamine related disorders)

IT Alzheimer's disease
Anti-Alzheimer's agents
Anti-inflammatory agents
Antidepressants
Antiparkinsonian agents
Antipsychotics
Anxiety
Anxiolytics
Cardiovascular agents
Cardiovascular system, disease
Dopamine agonists
Human
Inflammation
Parkinson's disease
Schizophrenia
(preparation of (heterocyclylalkyl)benzimidazole dopamine agonists for treatment of sexual dysfunction and other dopamine related disorders)

IT Drug delivery systems
(prodrugs; preparation of (heterocyclylalkyl)benzimidazole dopamine agonists for treatment of sexual dysfunction and other dopamine related disorders)

IT 70006-24-5P, 2-[[4-(Pyridin-2-yl)**piperazin**-1-yl]methyl]-1H-benzimidazole
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(dopamine agonist; preparation of (heterocyclylalkyl)benzimidazoles from heterocycles and (haloalkyl)benzimidazoles for treatment of sexual dysfunction)

IT 70006-20-1P, 2-[(4-**Phenylpiperazin**-1-yl)methyl]-1H-benzimidazole
70006-22-3P, 2-[[4-(2-Methoxyphenyl)**piperazin**
-1-yl]methyl]-1H-benzimidazole 70006-25-6P, 2-[[4-(**1,3**
-**Thiazol**-2-yl)**piperazin**-1-yl]methyl]-1H-benzimidazole
159557-22-9P, 2-[(4-Phenyl-3,6-dihydropyridin-1(2H)-yl)methyl]-1H-
benzimidazole 474417-17-9P, 2-[[4-(Pyridin-2-yl)**piperazin**
-1-yl]methyl]-1H-benzimidazole maleate (1:1) 474417-18-0P,
2-[[4-(Pyrimidin-2-yl)**piperazin**-1-yl]methyl]-1H-benzimidazole
474417-19-1P, 2-[[4-(6-Methylpyridin-2-yl)**piperazin**
-1-yl]methyl]-1H-benzimidazole 474417-20-4P, 2-[4-[(1H-Benzimidazol-2-
yl)methyl]**piperazin**-1-yl]nicotinonitrile 474417-21-5P,
5,7-Dibromo-2-[[4-(pyridin-2-yl)**piperazin**-1-yl]methyl]-1H-
benzimidazole 474417-22-6P, 5-Fluoro-2-[[4-(pyridin-2-yl)
piperazin-1-yl]methyl]-1H-benzimidazole 474417-24-8P, Isobutyl
2-[[4-(pyridin-2-yl)**piperazin**-1-yl]methyl]-1H-benzimidazole-1-
carboxylate 474417-25-9P, 2-[[4-(Pyridin-2-yl)**piperazin**
-1-yl]methyl]-1-(pyrrolidin-1-ylcarbonyl)-1H-benzimidazole 474417-26-0P,
N,N-Dimethyl-2-[[4-(pyridin-2-yl)**piperazin**-1-yl]methyl]-1H-
benzimidazole-1-carboxamide 474417-27-1P, 2-[4-[(1H-Benzimidazol-2-
yl)methyl]**piperazin**-1-yl]benzonitrile 474417-28-2P,
2-[[4-(2-Chlorophenyl)**piperazin**-1-yl]methyl]-1H-benzimidazole
474417-29-3P, 2-[[4-(2-Fluorophenyl)**piperazin**
-1-yl]methyl]-1H-benzimidazole 474417-30-6P, 2-[[4-(2-Nitrophenyl)
piperazin-1-yl]methyl]-1H-benzimidazole 474417-31-7P,
2-[[4-(2-Nitrophenyl)**piperazin**-1-yl]methyl]-1H-benzimidazole
trifluoroacetate (1:1) 474417-32-8P, 4-[4-[(1H-Benzimidazol-2-yl)methyl]
piperazin-1-yl]phenol 474417-33-9P, 2-[[4-[2-(Methylthio)phenyl]
piperazin-1-yl]methyl]-1H-benzimidazole 474417-34-0P,
2-[[4-(2-Ethoxyphenyl)**piperazin**-1-yl]methyl]-1H-benzimidazole
474417-35-1P, 2-[4-[(1H-Benzimidazol-2-yl)methyl]**piperazin**
-1-yl]phenol 474417-36-2P, 2-[[4-(2-Methoxyphenyl)piperidin-1-yl]methyl]-
1H-benzimidazole 474417-37-3P, 2-[(4-Pyridin-2-ylpiperidin-1-yl)methyl]-
1H-benzimidazole 474417-39-5P, 2-[[2-Methyl-4-(pyridin-2-yl)
piperazin-1-yl]methyl]-1H-benzimidazole 474417-41-9P,
2-[[(2S)-2-Methyl-4-(pyridin-2-yl)**piperazin**-1-yl]methyl]-1H-
benzimidazole 474417-43-1P, 2-[[(2R)-2-Methyl-4-(pyridin-2-yl)
piperazin-1-yl]methyl]-1H-benzimidazole 474417-45-3P,
N-[2-[4-[(1H-Benzimidazol-2-yl)methyl]**piperazin**
-1-yl]pyridin-3-yl]methanesulfonamide 474417-47-5P, 2-[[4-(3-
Fluoropyridin-2-yl)**piperazin**-1-yl]methyl]-1H-benzimidazole
474417-48-6P, 6-[4-[(1H-Benzimidazol-2-yl)methyl]**piperazin**
-1-yl]pyridin-3-ol 474417-51-1P, 2-[[4-(3-Methylpyridin-2-yl)
piperazin-1-yl]methyl]-1H-benzimidazole 474417-52-2P
587870-75-5P 587870-76-6P 587870-77-7P 587870-78-8P 587870-79-9P
587870-80-2P 587870-81-3P 587870-82-4P 587870-83-5P 587870-84-6P
587870-85-7P 587870-86-8P 587870-87-9P 587870-88-0P 587870-89-1P
587870-90-4P 587870-91-5P 587870-92-6P 587870-93-7P 587870-94-8P
587870-95-9P 587870-96-0P 587870-97-1P 587870-98-2P 587870-99-3P
587871-00-9P 587871-01-0P 587871-02-1P 587871-03-2P 587871-04-3P
587871-05-4P 587871-06-5P 587871-07-6P 587871-08-7P 587871-09-8P
587871-10-1P 587871-11-2P 587871-12-3P 587871-13-4P 587871-14-5P
587871-15-6P 587871-16-7P 587871-17-8P 587871-18-9P 587871-19-0P
587871-20-3P 587871-21-4P 587871-22-5P 587871-23-6P 587871-24-7P
587871-25-8P 587871-27-0P 587871-29-2P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
(Uses)
(dopamine agonist; preparation of (heterocyclylalkyl)benzimidazoles from
heterocycles and (haloalkyl)benzimidazoles for treatment of sexual
dysfunction)

IT 9068-52-4, Phosphodiesterase 5
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitor, coadministration; preparation of (heterocyclylalkyl)benzimidazol

e dopamine agonists for treatment of sexual dysfunction and other dopamine related disorders)

IT 17282-04-1P, 2-Chloro-3-fluoropyridine 30532-37-7P, 4-(Pyrid-2-yl)piperidine 42270-37-1P, 1-(2-Thiazolyl)**piperazine** 84611-43-8P, 5-(Benzyloxy)-2-chloropyridine 85386-84-1P, 1-(3-Fluoropyridin-2-yl)**piperazine** 156144-42-2P, 5-Fluoro-2-chloromethylbenzimidazole 158955-23-8P, N-(2-Chloropyridin-3-yl)methanesulfonamide 161610-16-8P, Benzyl 4-hydroxy-4-pyridin-2-ylpiperidine-1-carboxylate 474417-23-7P, 1-(2-Thiazolyl)-4-(tert-butoxycarbonyl)**piperazine** 474417-40-8P, 3-Methyl-1-(pyridin-2-yl)**piperazine** hydrobromide 474417-42-0P, (3S)-3-Methyl-1-pyridin-2-**ylpiperazine** 474417-44-2P, (3R)-3-Methyl-1-pyridin-2-**ylpiperazine** 474417-46-4P, N-(2-**Piperazin**-1-ylpyridin-3-yl)methanesulfonamide 474417-49-7P, tert-Butyl 4-[5-(benzyloxy)pyridin-2-yl]**piperazine**-1-carboxylate 474417-50-0P, 2-[[4-[5-(Benzyloxy)pyridin-2-yl]**piperazin**-1-yl]methyl]-1H-benzimidazole
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of (heterocyclylalkyl)benzimidazoles from heterocycles and (haloalkyl)benzimidazoles for treatment of sexual dysfunction)

IT 587870-74-4P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of (heterocyclylalkyl)benzimidazoles from heterocycles and (haloalkyl)benzimidazoles for treatment of sexual dysfunction)

IT 79-44-7, N,N-Dimethylcarbamoyl chloride 92-54-6, 1-**Phenylpiperazine** 100-39-0, Benzyl bromide 109-04-6, 2-Bromopyridine 109-07-9, 2-**Methylpiperazine** 110-85-0, **Piperazine**, reactions 367-31-7, 4-Fluoro-1,2-phenylenediamine 372-47-4, 3-Fluoropyridine 543-27-1, Isobutyl chloroformate 1011-15-0, 1-(2-Fluorophenyl)**piperazine** 1011-17-2, 1-(2-Hydroxyphenyl)**piperazine** 1013-24-7, 1-(2-Methylthiophenyl)**piperazine** 1192-63-8, 1-Pyrrolidinecarbonyl chloride 1575-38-8, 4,6-Dibromo-1,2-phenylenediamine 3034-53-5, 2-Bromothiazole 4857-04-9, 2-Chloromethylbenzimidazole 4857-06-1, 2-Chlorobenzimidazole 6298-19-7, 2-Chloropyridin-3-ylamine 13339-01-0, 1-(2-Ethoxyphenyl)**piperazine** 19099-93-5, Benzyl 4-oxo-1-piperidine carboxylate 20980-22-7, 1-(2-Pyrimidyl)**piperazine** 34803-66-2, 1-(2-Pyridyl)**piperazine** 35386-24-4, 1-(2-Methoxyphenyl)**piperazine** 39512-50-0, 1-(2-Chlorophenyl)**piperazine** 41288-96-4, 2-Chloro-5-hydroxypyridine 43064-12-6, 4-Phenyl-1,2,3,6-tetrahydropyridine hydrochloride 55745-89-6, 1-(6-Methylpyridin-2-yl)**piperazine** 56621-48-8, 1-(4-Hydroxyphenyl)**piperazine** 57260-71-6, tert-Butyl 1-**piperazinecarboxylate** 58333-75-8, 4-(2-Methoxyphenyl)piperidine 59084-06-9, 1-(2-Nitrophenyl)**piperazine** 74879-18-8, (S)-2-**Methylpiperazine** 75336-86-6, (R)-2-**Methylpiperazine** 84951-44-0, 1-(3-Cyanopyridin-2-yl)**piperazine** 111373-03-6, 1-(2-Cyanophenyl)**piperazine**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of (heterocyclylalkyl)benzimidazoles from heterocycles and (haloalkyl)benzimidazoles for treatment of sexual dysfunction)

L28 ANSWER 3 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:370793 CAPLUS
DOCUMENT NUMBER: 140:370818
TITLE: Benzodiazepinone inhibitors of cyclic nucleotide phosphodiesterase PDE2 for use in treatment of nervous system disorders
INVENTOR(S): Bourguignon, Jean Jacques; Lugnier, Claire; Abarghaz,

Mustapha; Lagouge, Yan; Wagner, Patrick; Mondadori, Cesare; Macher, Jean Paul; Schultz, Dominique; Raboisson, Pierre

PATENT ASSIGNEE(S): Neuro3d, Fr.

SOURCE: Fr. Demande, 126 pp.
CODEN: FRXXBL

DOCUMENT TYPE: Patent

LANGUAGE: French

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
FR 2846653	A1	20040507	FR 2002-13607	20021030
WO 2004041258	A2	20040521	WO 2003-FR3247	20031030
WO 2004041258	A3	20040923		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:

FR 2002-13607	A	20021030
US 2003-455874P	P	20030320

OTHER SOURCE(S): MARPAT 140:370818

AN 2004:370793 CAPLUS

DN 140:370818

ED Entered STN: 07 May 2004

TI Benzodiazepinone inhibitors of cyclic nucleotide phosphodiesterase PDE2 for use in treatment of nervous system disorders

IN Bourguignon, Jean Jacques; Lugnier, Claire; Abarghaz, Mustapha; Lagouge, Yan; Wagner, Patrick; Mondadori, Cesare; Macher, Jean Paul; Schultz, Dominique; Raboisson, Pierre

PA Neuro3d, Fr.

SO Fr. Demande, 126 pp.
CODEN: FRXXBL

DT Patent

LA French

IC ICM C07D401-04
ICS C07D243-24; C07D243-22; C07D243-14; A61K031-5513; A61P025-28; A61P025-22; A61P025-24; A61P003-04; A61P025-00; A61P013-00; A61P001-16; A61P037-08; A61P019-02; C07D213-04

CC 7-3 (Enzymes)

FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	FR 2846653	A1	20040507	FR 2002-13607	20021030
	WO 2004041258	A2	20040521	WO 2003-FR3247	20031030
	WO 2004041258	A3	20040923		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI FR 2002-13607 A 20021030
US 2003-455874P P 20030320

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
FR 2846653	ICM	C07D401-04
	ICS	C07D243-24; C07D243-22; C07D243-14; A61K031-5513; A61P025-28; A61P025-22; A61P025-24; A61P003-04; A61P025-00; A61P013-00; A61P001-16; A61P037-08; A61P019-02; C07D213-04
FR 2846653	ECLA	A61K031/5513

OS MARPAT 140:370818

AB The invention relates to benzodiazepinone inhibitors of PDE2 and their use in treatment of disorders of the central and peripheral nervous system. Thus, 7,8-dimethyl-1-Me 5-[3-(4-phenyl-**1,3-thiazol**-2-yl)phenyl]-1,3-dihydro-2H-1,4-benzodiazepin-2-one was synthesized. This compound inhibited the in vitro activity of bovine smooth muscle PDE2 by 91.4% at 10 μM.

ST benzodiazepinone inhibitor cyclic nucleotide phosphodiesterase nervous system disorder

IT Brain, disease
(Gilles de la Tourette syndrome; benzodiazepinone inhibitors of cyclic nucleotide phosphodiesterase PDE2 for use in treatment of nervous system disorders)

IT Nervous system, disease
(amyotrophic lateral sclerosis; benzodiazepinone inhibitors of cyclic nucleotide phosphodiesterase PDE2 for use in treatment of nervous system disorders)

IT Mental disorder
(attention deficit disorder; benzodiazepinone inhibitors of cyclic nucleotide phosphodiesterase PDE2 for use in treatment of nervous system disorders)

IT Allergy
Allergy inhibitors
Alzheimer's disease
Anti-Alzheimer's agents
Antiasthmatics
Anticonvulsants
Antidepressants
Antiobesity agents
Antiparkinsonian agents
Antipsychotics
Antirheumatic agents
Anxiety
Anxiolytics
Asthma
Autoimmune disease
Drug dependence
Epilepsy
Liver, disease
Multiple sclerosis
Nervous system, disease
Obesity
Parkinson's disease
Rheumatic diseases
Rheumatoid arthritis
Schizophrenia
(benzodiazepinone inhibitors of cyclic nucleotide phosphodiesterase PDE2 for use in treatment of nervous system disorders)

IT Mental disorder
(bipolar disorder; benzodiazepinone inhibitors of cyclic nucleotide phosphodiesterase PDE2 for use in treatment of nervous system disorders)

RE.CNT 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) American Home Prod; GB 1346176 A 1974 CAPLUS
(2) Cassella Farbwerke Mainkur Ag; DE 1942744 A 1971 CAPLUS
(3) Francoise, B; WO 9958117 A 1999 CAPLUS
(4) Fryer, R; J ORG CHEM 1970, V35(7), P2455
(5) Hasegawa, H; JP 45031303 B 1970 CAPLUS
(6) Hirohashi, T; US 3778433 A 1973 CAPLUS
(7) Houlihan, W; US 3609146 A 1971 CAPLUS
(8) Kolbach, G; HELVETICA CHIMICA ACTA 1977, V60(1), P265
(9) La Roche, H; DE 1136709 B 1962 CAPLUS
(10) La Roche, H; DE 1145626 B 1963 CAPLUS
(11) McCaully, R; US 3803129 A 1974 CAPLUS
(12) Nakai, H; JP 44026871 B 1969 CAPLUS
(13) Parfitt, K; Martindale The Complete Drug Reference 1999
(14) Schultz, D; WO 02098865 A 2002 CAPLUS
(15) Stempel, A; US 3515755 A 1970 CAPLUS
(16) Sternbach, L; J ORG CHEM 1962, V27, P3788 CAPLUS
(17) Sumitomo Chemical Company Ltd; DE 2017060 A 1970 CAPLUS
(18) Szmuszkovicz, J; US 3573282 A 1971 CAPLUS
(19) Tamura, Y; JP 54157585 A 1979 CAPLUS
(20) Teller, D; US 4056525 A 1977 CAPLUS
(21) Waldeck, H; US 5010076 A 1991 CAPLUS

L28 ANSWER 4 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:41473 CAPLUS
DOCUMENT NUMBER: 140:94069
TITLE: Preparation of imidazotriazines as selective phosphodiesterase-10a inhibitors for the treatment of cancer and neurodegenerative diseases
INVENTOR(S): Niewoehner, Ulrich; Hendrix, Martin; Brueckner, David; Friedl, Arno; Gerlach, Irene; Hinz, Volker; Keldenich, Joerg; Mauler, Frank; Schauss, Dagmar; Schlemmer, Karl-heinz; Tersteegen, Adrian; Yalkinoglu, Oezkan
PATENT ASSIGNEE(S): Bayer Healthcare Ag, Germany; Niewoehner, Maria; et al.
SOURCE: PCT Int. Appl., 92 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004005291	A1	20040115	WO 2003-EP6662	20030625
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10230604	A1	20040129	DE 2002-10230604	20020708
PRIORITY APPLN. INFO.:			DE 2002-10230604 A	20020708

OTHER SOURCE(S): MARPAT 140:94069
AN 2004:41473 CAPLUS
DN 140:94069
ED Entered STN: 18 Jan 2004
TI Preparation of imidazotriazines as selective phosphodiesterase-10a

inhibitors for the treatment of cancer and neurodegenerative diseases

IN Niewoehner, Ulrich; Hendrix, Martin; Brueckner, David; Friedl, Arno; Gerlach, Irene; Hinz, Volker; Keldenich, Joerg; Mauler, Frank; Schauss, Dagmar; Schlemmer, Karl-heinz; Tersteegen, Adrian; Yalkinoglu, Oezkan

PA Bayer Healthcare Ag, Germany; Niewoehner, Maria; et al.

SO PCT Int. Appl., 92 pp.
CODEN: PIXXD2

DT Patent

LA German

IC ICM C07D487-04
ICS A61K031-53; A61P025-16; A61P025-18; C07D253-00; C07D235-00

CC 28-19 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1

FAN.CNT 1

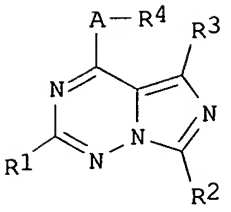
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2004005291	A1	20040115	WO 2003-EP6662	20030625
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10230604	A1	20040129	DE 2002-10230604	20020708
PRAI DE 2002-10230604	A	20020708		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2004005291	ICM	C07D487-04
	ICS	A61K031-53; A61P025-16; A61P025-18; C07D253-00; C07D235-00
DE 10230604	ECLA	A61K031/53; C07D487/04+253C+235C

OS MARPAT 140:94069

GI



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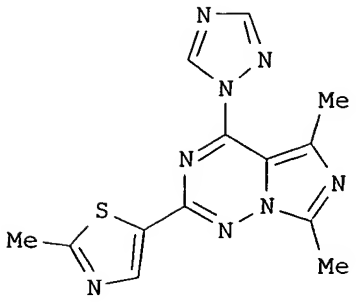
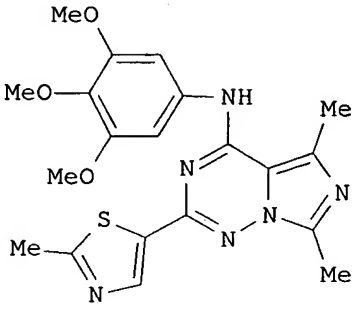


II



III

AB Title compds. I [R1 = (un)substituted heteroaryl; R2 = alkyl, cycloalkyl; R3 = Me; A = O, NH; R4 = (un)substituted aryl, e.g., halo, CHO, CO2H, etc.] and their pharmaceutically acceptable salts were prepared For example, condensation of triazine II and 3,4,5-trimethoxyaniline afforded imidazotriazine III in 65% yield. In phosphodiesterase-10a inhibition assays, 5-examples of compds. I exhibited IC50 values ranging from 8-150 nM, e.g., the IC50 value of imidazotriazine III was 93 nM. Compds. I are claimed useful for the treatment of cancer and neurodegenerative diseases.

ST imidazotriazine prepn dakin west acylation; neurodegenerative disease imidazotriazine prepn; anticancer agent imidazotriazine prepn; psychotherapeutic agent imidazotriazine prepn; antiparkinsonian agent imidazotriazine prepn

IT Acylation
(Dakin-West, isoform a; preparation of imidazotriazines as selective phosphodiesterase-10a inhibitors for the treatment of cancer and neurodegenerative diseases)

IT Nervous system, disease
(degeneration, treatment of; preparation of imidazotriazines as selective phosphodiesterase-10a inhibitors for the treatment of cancer and neurodegenerative diseases)

IT Antiparkinsonian agents
Antipsychotics
Antitumor agents
Human
Nervous system agents
Psychotropics
(preparation of imidazotriazines as selective phosphodiesterase-10a inhibitors for the treatment of cancer and neurodegenerative diseases)

IT Mental disorder
Neoplasm
Parkinson's disease
Schizophrenia
(treatment of; preparation of imidazotriazines as selective phosphodiesterase-10a inhibitors for the treatment of cancer and neurodegenerative diseases)

IT 51528-02-0P 110347-55-2P 201937-23-7P 644976-08-9P 644976-09-0P
644976-10-3P 644976-11-4P 644976-12-5P 644976-13-6P 644976-14-7P
644976-16-9P 644976-17-0P 644976-18-1P 644976-19-2P 644976-20-5P
644976-21-6P 644976-22-7P 644976-23-8P 644976-24-9P 644976-25-0P
644976-26-1P 644976-27-2P 644976-28-3P 644976-29-4P 644976-30-7P
644976-31-8P 644976-32-9P 644976-33-0P 644976-34-1P 644976-35-2P
644976-36-3P 644976-37-4P 644976-38-5P 644976-39-6P 644976-40-9P
644976-41-0P 644976-43-2P 644976-44-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of imidazotriazines as selective phosphodiesterase-10a inhibitors for the treatment of cancer and neurodegenerative diseases)

IT 9040-59-9
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(isoform a; preparation of imidazotriazines as selective phosphodiesterase-10a inhibitors for the treatment of cancer and neurodegenerative diseases)

IT 67-56-1, Methanol, reactions 78-84-2 110-91-8, **Morpholine**, reactions 288-88-0, 1,2,4-Triazole 642-71-7, 3,4,5-Trimethoxyphenol 937-14-4, Mcpba 1115-69-1 1641-09-4, 3-Thiophencarbonitrile 4755-77-5, Ethyloxalylchloride 5470-70-2, Methyl 6-methylnicotinate 7803-57-8, Hydrazine hydrate 24313-88-0, 3,4,5-Trimethoxyaniline 29681-45-6, Methyl 5-methylnicotinate 54610-69-4, 2-Furancarboximidamide hydrochloride 61097-49-2, 2-Pyridinecarboximidamide hydrochloride 73781-91-6, 6-Chloro-3-pyridinecarboxylic acid methyl ester 449175-50-2, 2-Methyl-**1,3-thiazol**-5-carboximidamide hydrochloride 454426-80-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of imidazotriazines as selective phosphodiesterase-10a inhibitors for the treatment of cancer and neurodegenerative diseases)

IT 644975-80-4P 644975-81-5P 644975-82-6P 644975-83-7P 644975-84-8P
644975-85-9P 644975-86-0P 644975-87-1P 644975-88-2P 644975-89-3P
644975-90-6P 644975-91-7P 644975-92-8P 644975-93-9P 644975-94-0P
644975-95-1P 644975-96-2P 644975-97-3P 644975-98-4P 644975-99-5P
644976-00-1P 644976-01-2P 644976-02-3P 644976-04-5P 644976-05-6P
644976-06-7P 644976-07-8P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(target compound; preparation of imidazotriazines as selective phosphodiesterase-10a inhibitors for the treatment of cancer and neurodegenerative diseases)

RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Bayer Ag; DE 10130151 A 2003 CAPLUS
(2) Bayer Ag; DE 10130167 A 2003 CAPLUS
(3) Clarke; US 3941785 A 1976 CAPLUS
(4) Jens-Kerim, E; WO 0248144 A 2002 CAPLUS
(5) Pfizer Prod Inc; EP 1250923 A 2002 CAPLUS

L28 ANSWER 5 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:972080 CAPLUS
DOCUMENT NUMBER: 140:27845
TITLE: Fused bicyclic aromatic compounds with dopamine D4 receptor agonist activity that are useful in treating sexual dysfunction, and their preparation and use
INVENTOR(S): Cowart, Marlon D.
PATENT ASSIGNEE(S): Abbott Laboratories, USA
SOURCE: PCT Int. Appl., 149 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2003101994	A1	20031211	WO 2003-US16878		20030529
W: CA, JP, MX					
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR					
US 2004002488	A1	20040101	US 2002-158370		20020529
US 2004063713	A1	20040401	US 2003-443814		20030523
PRIORITY APPLN. INFO.:			US 2002-158370	A	20020529
			US 2003-443814	A	20030523
			US 2002-384291P	P	20020529

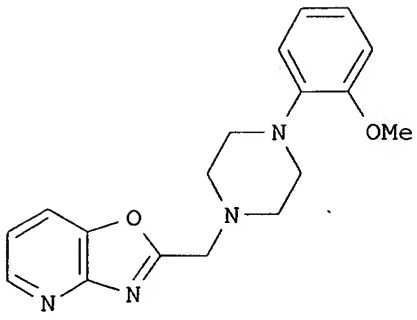
OTHER SOURCE(S): MARPAT 140:27845
AN 2003:972080 CAPLUS
DN 140:27845
ED Entered STN: 14 Dec 2003
TI Fused bicyclic aromatic compounds with dopamine D4 receptor agonist activity that are useful in treating sexual dysfunction, and their preparation and use
IN Cowart, Marlon D.
PA Abbott Laboratories, USA
SO PCT Int. Appl., 149 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07D491-04
ICS C07D513-04; C07D495-04; C07D498-04; A61P015-10; A61K031-495
CC 28-17 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 63
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003101994	A1	20031211	WO 2003-US16878	20030529
	W: CA, JP, MX				
	RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR				
	US 2004002488	A1	20040101	US 2002-158370	20020529
	US 2004063713	A1	20040401	US 2003-443814	20030523
PRAI	US 2002-158370	A	20020529		
	US 2003-443814	A	20030523		
	US 2002-384291P	P	20020529		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2003101994	ICM	C07D491-04
	ICS	C07D513-04; C07D495-04; C07D498-04; A61P015-10; A61K031-495

OS MARPAT 140:27845
GI



II

AB The invention relates to the use of title compds. A-L-D-B1 (I) for the treatment of sexual dysfunction, and to compns. containing compds. I for such treatment [wherein: A = various (un)substituted 6/5- and 5/5-fused bicyclic aromatic nuclei, including indole, benzothiophene, pyrrolopyridine, oxazolopyridine, thiazolopyridine, and thienoimidazole; L = alkylene; D = (un)substituted 1,4-piperidinediyl, 1,2,5,6-tetrahydropyridine-1,4-diyl, 1,4-(homo)**piperazinediyl**, 2,5-diazabicyclo[2.2.1]heptane-2,5-diyl; B1 = (un)substituted Ph, 2-pyridinyl, 1-oxy-2-pyridinyl, 2-pyrimidinyl, 6-oxopyridazin-1-yl, various azol-2-yls, 2-furyl, 2-thienyl; with 1 excluded compound]. The compds. are centrally active dopamine D4 receptor agonists. Claimed uses are primarily for treatment of male and female sexual dysfunction, especially male erectile dysfunction, as well as other conditions, including cardiovascular, inflammatory, and various CNS disorders. Approx. 70 compds. I and a variety of intermediates were prepared For instance, cyclocondensation of 2-amino-3-pyridinol with ClCH2C(OMe)3 in diglyme in the presence of p-MeC6H4SO3H at 80° gave 2-(chloromethyl)-[1,3]oxazolo[4,5-b]pyridine, which was aminated with 1-(2-methoxyphenyl)**piperazine** in MeCN to give invention compound II. In a functional test against human D4 receptor expressed in a stable HEK-293 cell line, representative compds. I exhibited EC50 values (vs. 10 μM dopamine) in the range of 7.5 nM to 3800 nM. In a rat penile erection model, representative compds. I at 0.01-1.0 μmol/kg s.c. gave at least 30% incidence of erection(s) during 1 h after administration.

ST fused bicyclic arom prepn dopamine D4 receptor agonist; **piperazine** piperidine bicyclic heteroarylmethyl prepn treatment sexual dysfunction; penile erection stimulant D4 agonist fused bicyclic arom compd

IT Dopamine agonists
(D4; preparation of fused bicyclic aromatic compds. as dopamine D4 agonists for
treatment of sexual dysfunction)

IT Dopamine receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(D4; preparation of fused bicyclic aromatic compds. as dopamine D4 agonists for
treatment of sexual dysfunction)

IT Drugs of abuse
(abuse of, treatment of; preparation of fused bicyclic aromatic compds. as dopamine D4 agonists for treatment of sexual dysfunction)

IT Sexual behavior
(aphrodisiacs for; preparation of fused bicyclic aromatic compds. as dopamine
D4 agonists for treatment of sexual dysfunction)

IT Heterocyclic compounds
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(aromatic; preparation of fused bicyclic aromatic compds. as dopamine D4 agonists

for treatment of sexual dysfunction)
IT Mental disorder
(attention deficit hyperactivity disorder, treatment of; preparation of fused bicyclic aromatic compds. as dopamine D4 agonists for treatment of sexual dysfunction)
IT Adrenoceptor antagonists
Dopamine agonists
(combination treatment with; preparation of fused bicyclic aromatic compds. as
dopamine D4 agonists for treatment of sexual dysfunction)
IT Mental disorder
(depression, treatment of; preparation of fused bicyclic aromatic compds. as dopamine D4 agonists for treatment of sexual dysfunction)
IT Sexual behavior
(disorder, female, treatment of; preparation of fused bicyclic aromatic compds.
as dopamine D4 agonists for treatment of sexual dysfunction)
IT Sexual behavior
(disorder, treatment of; preparation of fused bicyclic aromatic compds. as dopamine D4 agonists for treatment of sexual dysfunction)
IT Aromatic compounds
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(heterocyclic; preparation of fused bicyclic aromatic compds. as dopamine D4 agonists for treatment of sexual dysfunction)
IT Sexual behavior
(impotence, treatment of; preparation of fused bicyclic aromatic compds. as dopamine D4 agonists for treatment of sexual dysfunction)
IT Mental disorder
(mood-affecting, treatment of; preparation of fused bicyclic aromatic compds.
as dopamine D4 agonists for treatment of sexual dysfunction)
IT Sexual behavior
(penile erection, stimulation of; preparation of fused bicyclic aromatic compds. as dopamine D4 agonists for treatment of sexual dysfunction)
IT Anti-Alzheimer's agents
Anti-inflammatory agents
Antidepressants
Antiparkinsonian agents
Antipsychotics
Anxiolytics
Cardiovascular agents
Human
(preparation of fused bicyclic aromatic compds. as dopamine D4 agonists for treatment of sexual dysfunction)
IT Alzheimer's disease
Anxiety
Cardiovascular system, disease
Inflammation
Parkinson's disease
Schizophrenia
(treatment of; preparation of fused bicyclic aromatic compds. as dopamine D4 agonists for treatment of sexual dysfunction)
IT 220941-93-5P, 5-Fluoro-2-[[4-(2-pyridinyl)-1-**piperazinyl**]methyl]-1H-indole 632333-51-8P, 2-[1-[(5-Chloro-1-benzothien-3-yl)methyl]-4-piperidinyl]pyridine 632333-52-9P, 1-[(5-Chloro-1-benzothien-3-yl)methyl]-4-(6-methyl-2-pyridinyl)**piperazine** 632333-53-0P, 2-[4-[(5-Chloro-1-benzothien-3-yl)methyl]-1-**piperazinyl**]benzonitrile 632333-54-1P, 1-[(5-Chloro-1-benzothien-3-yl)methyl]-4-(2-pyridinyl)**piperazine** 632333-55-2P, 1-[(5-Chloro-1-benzothien-3-yl)methyl]-4-(2-fluorophenyl)**piperazine** 632333-56-3P, 2-[4-[(5-Chloro-1-benzothien-3-

yl)methyl]-1-**piperazinyl**]pyrimidine 632333-57-4P, 1-(1-Benzothien-3-ylmethyl)-4-(2-pyridinyl)**piperazine** 632333-58-5P, 2-[4-(1-Benzothien-2-ylmethyl)-1-**piperazinyl**]benzonitrile 632333-60-9P, 1-(1-Benzothien-2-ylmethyl)-4-(2-fluorophenyl)**piperazine** 632333-62-1P, 1-(1-Benzothien-2-ylmethyl)-4-(2-pyridinyl)**piperazine** 632333-64-3P, 2-[4-[(5-Fluoro-1H-indol-2-yl)methyl]-1,4-diazepan-1-yl]benzonitrile 632333-66-5P, 2-[1-[4-(2-Methoxyphenyl)-1-**piperazinyl**]ethyl]-1H-indole 632333-68-7P, 2-[[4-(2-Methoxyphenyl)-1-**piperazinyl**]methyl]-1-methyl-1H-indole 632333-70-1P, 2-[1-[4-(2-Pyridinyl)-1-**piperazinyl**]ethyl]-1H-indole 632333-72-3P, 5-Fluoro-2-[[(1S,4S)-5-(2-pyridinyl)-2,5-diazabicyclo[2.2.1]hept-2-yl]methyl]-1H-indole 632333-73-4P, 5-Fluoro-2-[[4-(2-pyridinyl)-1,4-diazepan-1-yl]methyl]-1H-indole 632333-75-6P, 2-[4-(1H-Pyrrolo[2,3-b]pyridin-2-ylmethyl)-1-**piperazinyl**]benzonitrile 632333-77-8P, 2-[[4-(2-Pyrimidinyl)-1-**piperazinyl**]methyl]-1H-pyrrolo[2,3-b]pyridine 632333-78-9P, 2-[[4-(2-Methoxyphenyl)-1-**piperazinyl**]methyl]-1H-pyrrolo[2,3-b]pyridine 632333-79-0P, 2-[[4-(2-Pyridinyl)-1-**piperazinyl**]methyl]-1H-pyrrolo[2,3-b]pyridine 632333-80-3P, 2-[(4-Phenyl-1-**piperazinyl**)methyl]-1H-pyrrolo[2,3-b]pyridine 632333-82-5P, 2-[[4-(2-Fluorophenyl)-1-**piperazinyl**]methyl]-1H-pyrrolo[2,3-b]pyridine 632333-84-7P, 2-[4-(1H-Pyrrolo[2,3-b]pyridin-2-ylmethyl)-1-**piperazinyl**]nicotinonitrile 632333-86-9P, 4-[4-[[6-(Trifluoromethyl)thieno[3,2-b]pyridin-2-yl]methyl]-1-**piperazinyl**]phenol 632333-87-0P, 2-[[4-(2-Methoxyphenyl)-1-**piperazinyl**]methyl]-6-(trifluoromethyl)thieno[3,2-b]pyridine 632333-88-1P, 2-[4-[[6-(Trifluoromethyl)thieno[3,2-b]pyridin-2-yl]methyl]-1-**piperazinyl**]benzonitrile 632333-89-2P, 4-[4-(Furo[3,2-b]pyridin-2-ylmethyl)-1-**piperazinyl**]phenol 632333-90-5P, 2-[(4-Phenyl-1-**piperazinyl**)methyl]furo[3,2-b]pyridine 632333-91-6P, 2-[[4-(2-Methoxyphenyl)-1-**piperazinyl**]methyl]furo[3,2-b]pyridine 632333-92-7P, 2-[4-(Furo[3,2-b]pyridin-2-ylmethyl)-1-**piperazinyl**]benzonitrile 632333-93-8P, 2-[[4-(3-Methyl-2-pyridinyl)-1-**piperazinyl**]methyl]furo[3,2-b]pyridine 632333-94-9P, 2-[4-(Furo[3,2-b]pyridin-2-ylmethyl)-1-**piperazinyl**]nicotinonitrile 632333-95-0P, 2-[[4-(2-Pyridinyl)-1-**piperazinyl**]methyl]furo[3,2-b]pyridine 632333-96-1P, 2-[[4-(2-Fluorophenyl)-1-**piperazinyl**]methyl]furo[3,2-b]pyridine 632333-97-2P, 2-[[4-(2-Methoxyphenyl)-1-**piperazinyl**]methyl]-[1,3]oxazolo[4,5-b]pyridine 632333-98-3P, 2-[4-([1,3]Oxazolo[4,5-b]pyridin-2-ylmethyl)-1-**piperazinyl**]benzonitrile 632333-99-4P, 2-[[4-(2-Pyridinyl)-1-piperidinyl]methyl]-[1,3]thiazolo[5,4-b]pyridine 632334-01-1P, 2-[[4-(**1,3-Thiazol**-2-yl)-1-**piperazinyl**]methyl][1,3]thiazolo[5,4-b]pyridine 632334-03-3P, 4-[4-[(5-Methoxy-[1,3]thiazolo[5,4-b]pyridin-2-yl)methyl]-1-**piperazinyl**]phenol 632334-05-5P, 2-[[4-(2-Fluorophenyl)-1-**piperazinyl**]methyl]-5-methoxy-[1,3]thiazolo[5,4-b]pyridine 632334-07-7P, 5-Methoxy-2-[[4-[2-(methylthio)phenyl]-1-**piperazinyl**]methyl][1,3]thiazolo[5,4-b]pyridine 632334-09-9P, 5-Methoxy-2-[[4-(6-methyl-2-pyridinyl)-1-**piperazinyl**]methyl][1,3]thiazolo[5,4-b]pyridine 632334-11-3P, 5-Methoxy-2-[[4-(2-pyridinyl)-1-**piperazinyl**]methyl]-[1,3]thiazolo[5,4-b]pyridine 632334-13-5P, 5-Methoxy-2-[[4-(2-pyrimidinyl)-1-**piperazinyl**]methyl]-[1,3]thiazolo[5,4-b]pyridine 632334-15-7P, 5-Methoxy-2-[[4-(2-methoxyphenyl)-1-**piperazinyl**]methyl]-[1,3]thiazolo[5,4-b]pyridine 632334-17-9P, 2-[[4-(2-Chlorophenyl)-1-**piperazinyl**]methyl]-5-methoxy-[1,3]thiazolo[5,4-b]pyridine 632334-19-1P, 2-[4-[[5-Methoxy[1,3]thiazolo[5,4-b]pyridin-2-yl]methyl]-1-**piperazinyl**]benzonitrile 632334-21-5P, 5-Methoxy-2-[(4-phenyl-1-**piperazinyl**)methyl][1,3]thiazolo[5,4-b]pyridine 632334-22-6P, 2-[[4-(2-Chlorophenyl)-1-**piperazinyl**]methyl][1,3]thiazolo[5,4-b]pyridine 632334-24-8P, 2-[[4-(6-Methyl-2-pyridinyl)-1-

piperazinyl]methyl][1,3]thiazolo[5,4-b]pyridine 632334-26-0P, 2-[[4-(5-Chloro-2-methoxyphenyl)-1-**piperazinyl**]methyl]-[1,3]thiazolo[5,4-b]pyridine 632334-27-1P, 4-[4-([1,3]Thiazolo[5,4-b]pyridin-2-ylmethyl)-1-**piperazinyl**]phenol 632334-28-2P, 2-[4-([1,3]Thiazolo[5,4-b]pyridin-2-ylmethyl)-1-**piperazinyl**]nicotinonitrile 632334-30-6P, 2-[[4-[2-(Methylthio)phenyl]-1-**piperazinyl**]methyl][1,3]thiazolo[5,4-b]pyridine 632334-31-7P, 2-[[4-(2-Pyrimidinyl)-1-**piperazinyl**]methyl][1,3]thiazolo[5,4-b]pyridine 632334-32-8P, 2-[[4-(2-Pyridinyl)-1-**piperazinyl**]methyl][1,3]thiazolo[5,4-b]pyridine 632334-34-0P, 2-[[4-(2-Fluorophenyl)-1-**piperazinyl**]methyl]-[1,3]thiazolo[5,4-b]pyridine 632334-36-2P, 2-[4-[[1,3]Thiazolo[5,4-b]pyridin-2-ylmethyl]-1-**piperazinyl**]benzonitrile 632334-38-4P, 2-[[4-(2-Methoxyphenyl)-1-**piperazinyl**]methyl]-[1,3]thiazolo[5,4-b]pyridine 632334-39-5P, 2-[(4-Phenyl-1-**piperazinyl**)methyl]-[1,3]thiazolo[5,4-b]pyridine 632334-40-8P, 2-[[4-(2-Fluorophenyl)-1-**piperazinyl**]methyl]-1H-thieno[3,4-d]imidazole 632334-42-0P, 2-[[4-(2-Methoxyphenyl)-1-**piperazinyl**]methyl]-1H-thieno[3,4-d]imidazole 632334-43-1P, 2-[[4-(2-Pyrimidinyl)-1-**piperazinyl**]methyl]-1H-thieno[3,4-d]imidazole 632334-45-3P, 2-[[4-(2-Pyridinyl)-1-**piperazinyl**]methyl]-1H-thieno[3,4-d]imidazole 632334-46-4P, 2-[4-(1H-Thieno[3,4-d]imidazol-2-ylmethyl)-1-**piperazinyl**]nicotinonitrile 632334-47-5P, 4-[4-(1H-Thieno[3,4-d]imidazol-2-ylmethyl)-1-**piperazinyl**]phenol 632334-48-6P, 2-[[4-[2-(Methylthio)phenyl]-1-**piperazinyl**]methyl]-1H-thieno[3,4-d]imidazole 632334-54-4P, 2-[4-[(5-Fluoro-1H-indol-2-yl)methyl]-1,4-diazepan-1-yl]benzonitrile maleate (1:2.4) 632334-59-9P, 5-Fluoro-2-[[(1S,4S)-5-(2-pyridinyl)-2,5-diazabicyclo[2.2.1]hept-2-yl]methyl]-1H-indole maleate (1:1.3) 632334-62-4P, 5-Fluoro-2-[[4-(2-pyridinyl)-1,4-diazepan-1-yl]methyl]-1H-indole maleate (1:1.2) 632334-63-5P, 5-Fluoro-2-[[4-(pyridin-2-yl)**piperazin**-1-yl]methyl]-1H-indole maleate (1:1)
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of fused bicyclic aromatic compds. as dopamine D4
agonists for treatment of sexual dysfunction)

IT 9068-52-4, Phosphodiesterase 5
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors, combination treatment with; preparation of fused bicyclic aromatic
compds. as dopamine D4 agonists for treatment of sexual dysfunction)

IT 17890-56-1P, 1-Benzothien-2-ylmethanol 90606-77-2P, 3',6'-Dihydro-2'H-[2,4']bipyridinyl-1'-carboxylic acid tert-butyl ester 108444-31-1P, 2-(Diethoxymethyl)furo[3,2-b]pyridine 110704-34-2P, 2-(Chloromethyl)-[1,3]oxazolo[4,5-b]pyridine 110704-35-3P, 2-(Chloromethyl)-[1,3]thiazolo[5,4-b]pyridine 112372-05-1P, Furo[3,2-b]pyridine-2-carboxaldehyde 138647-49-1P, 4-Trifluoromethanesulfonyloxy-3,6-dihydro-2H-pyridine-1-carboxylic acid tert-butyl ester 206446-49-3P, 3',4',5',6'-Tetrahydro-2'H-[2,4']bipyridinyl-1'-carboxylic acid tert-butyl ester 220941-96-8P, 5-Fluoro-2-[[4-(2-pyridinyl)-1-**piperazinyl**]carbonyl]-1H-indole 279250-32-7P, 1-Oxy-3',4',5',6'-tetrahydro-2'H-[2,4']bipyridinyl-1'-carboxylic acid tert-butyl ester 279250-33-8P, 1',2',3',4',5',6'-Hexahydro-[2,4']bipyridinyl 1-oxide 287114-32-3P, 1-(2-Pyridinyl)-1,4-diazepane 630118-28-4P, 1',2',3',4',5',6'-Hexahydro-[2,4']bipyridinyl 1-oxide hydrochloride 632334-51-1P, tert-Butyl 4-[(5-fluoro-1H-indol-2-yl)carbonyl]-1,4-diazepane-1-carboxylate 632334-52-2P, tert-Butyl 4-[(5-fluoro-1H-indol-2-yl)methyl]-1,4-diazepane-1-carboxylate 632334-53-3P, 2-(1,4-Diazepan-1-ylmethyl)-5-fluoro-1H-indole 632334-56-6P, tert-Butyl (1S,4S)-5-(2-pyridinyl)-2,5-diazabicyclo[2.2.1]heptane-2-carboxylate 632334-57-7P, (1S,4S)-2-(2-Pyridinyl)-2,5-diazabicyclo[2.2.1]heptane 632334-58-8P,

5-Fluoro-2-[[(1S,4S)-5-(2-pyridinyl)-2,5-diazabicyclo[2.2.1]hept-2-yl]carbonyl]-1H-indole 632334-60-2P, tert-Butyl 4-(2-pyridinyl)-1,4-diazepane-1-carboxylate 632334-61-3P, 5-Fluoro-2-[[4-(2-pyridinyl)-1,4-diazepan-1-yl]carbonyl]-1H-indole 632334-64-6P, Ethyl 6-(trifluoromethyl)thieno[3,2-b]pyridine-2-carboxylate 632334-65-7P, [6-(Trifluoromethyl)thieno[3,2-b]pyridin-2-yl]methanol 632334-66-8P, [6-(Trifluoromethyl)thieno[3,2-b]pyridin-2-yl]methyl methanesulfonate 632334-67-9P, 2-(Chloromethyl)-5-methoxy-[1,3]thiazolo[5,4-b]pyridine 632334-68-0P, 2-(Chloromethyl)-1H-thieno[3,4-d]imidazole
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of fused bicyclic aromatic compds. as dopamine D4 agonists for treatment of sexual dysfunction)

IT 92-54-6, 1-**Phenylpiperazine** 95-15-8, Benzothiophene 109-04-6, 2-Bromopyridine 271-63-6, 1H-Pyrrolo[2,3-b]pyridine 399-76-8, 5-Fluoro-1H-indole-2-carboxylic acid 623-51-8, Ethyl mercaptoacetate 1011-15-0, 1-(2-Fluorophenyl)**piperazine** 1013-24-7, 1-[2-(Methylthio)phenyl]**piperazine** 1198-51-2, 3-(Bromomethyl)-5-chloro-1-benzothiophene 2042-37-7, 2-Bromobenzonitrile 4264-35-1, 1-(1H-Indol-2-yl)ethanone 5381-20-4, 1-Benzothiophene-3-carboxaldehyde 10160-87-9, 3,3-Diethoxy-1-propyne 16867-03-1, 2-Amino-3-pyridinol 20980-22-7, 2-(1-**Piperazinyl**)pyrimidine 27421-51-8, 1-Methyl-1H-indole-2-carboxaldehyde 30532-37-7, 4-(2-Pyridyl)piperidine 34803-66-2, 1-(2-Pyridinyl)**piperazine** 35386-24-4, 1-(2-Methoxyphenyl)**piperazine** 38240-21-0, 3-Amino-2-pyridinethiol 39512-50-0, 1-(2-Chlorophenyl)**piperazine** 40263-57-8, 2-Iodo-3-pyridinol 42270-37-1 42362-14-1, 3-Amino-6-methoxy-2-pyridinethiol 51076-95-0, 2-Chloro-1,1,1-triethoxyethane 55745-89-6, 1-(6-Methyl-2-pyridinyl)**piperazine** 56621-48-8, 4-(1-**Piperazinyl**)phenol 74974-54-2, Trimethyl (chloromethyl)orthoformate 78637-85-1, 3,4-Thiophenediamine 79099-07-3, 1-(tert-Butoxycarbonyl)-4-piperidone 84951-44-0, 2-(1-**Piperazinyl**)nicotinonitrile 99857-72-4, 1-(5-Chloro-2-methoxyphenyl)**piperazine** 104396-10-3, 1-(3-Methyl-2-pyridinyl)**piperazine** 111373-03-6, 2-(1-**Piperazinyl**)benzonitrile 112275-50-0, tert-Butyl 1,4-diazepane-1-carboxylate 113451-59-5, tert-Butyl (1S,4S)-2,5-diazabicyclo[2.2.1]heptane-2-carboxylate 175277-50-6, 3-Chloro-5-(trifluoromethyl)-2-pyridinecarboxaldehyde 218777-23-2, 2-Pyridylzinc bromide
RL: RCT (Reactant); RACT (Reactant or reagent)
(starting material; preparation of fused bicyclic aromatic compds. as dopamine D4 agonists for treatment of sexual dysfunction)

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Frigola-Constansa, J; US 5182280 A 1993 CAPLUS
(2) Jozef, K; US 5792768 A 1998 CAPLUS
(3) Omori, K; WO 0119802 A 2001 CAPLUS

L28 ANSWER 6 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:757469 CAPLUS
DOCUMENT NUMBER: 139:276471
TITLE: Preparation of substituted amides as antagonists and/or inverse agonists of the cannabinoid-1 receptor for therapy
INVENTOR(S): Hagmann, William K.; Lin, Linus S.; Shah, Shrenik K.; Guthikonda, Ravindra N.; Qi, Hongbo; Chang, Linda L.; Liu, Ping; Armstrong, Helen M.; Jewell, James P.; Lanza, Thomas J., Jr.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA; et al.
SOURCE: PCT Int. Appl., 381 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003077847	A2	20030925	WO 2003-US7320	20030307
WO 2003077847	A3	20041104		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004058820	A1	20040325	US 2003-387265	20030312
PRIORITY APPLN. INFO.:			US 2002-363597P P	20020312
			US 2002-428351P P	20021122

OTHER SOURCE(S): MARPAT 139:276471
AN 2003:757469 CAPLUS
DN 139:276471
ED Entered STN: 26 Sep 2003
TI Preparation of substituted amides as antagonists and/or inverse agonists of the cannabinoid-1 receptor for therapy
IN Hagmann, William K.; Lin, Linus S.; Shah, Shrenik K.; Guthikonda, Ravindra N.; Qi, Hongbo; Chang, Linda L.; Liu, Ping; Armstrong, Helen M.; Jewell, James P.; Lanza, Thomas J., Jr.
PA Merck & Co., Inc., USA; et al.
SO PCT Int. Appl., 381 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K
CC 21-2 (General Organic Chemistry)
Section cross-reference(s): 1
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003077847	A2	20030925	WO 2003-US7320	20030307
	WO 2003077847	A3	20041104		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
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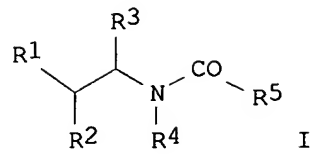
	US 2004058820	A1	20040325	US 2003-387265	20030312
PRAI	US 2002-363597P	P	20020312		
	US 2002-428351P	P	20021122		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2003077847	ICM	A61K

OS MARPAT 139:276471
GI



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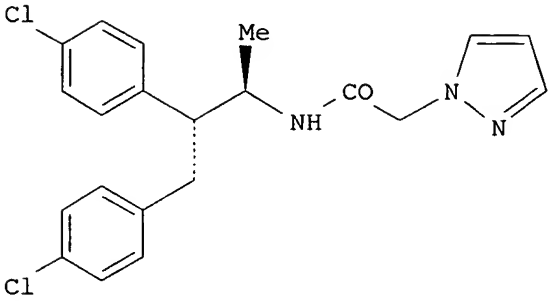

II

AB Novel compds. of the structural formula I (e.g. N-[2,3-bis(4-chlorophenyl)-1-methylpropyl]-2-(pyrazol-1-yl)acetamide trifluoroacetate (base shown as II with relative stereochem.); variables defined below) are antagonists and/or inverse agonists of the cannabinoid-1 (CB1) receptor (no data) and are useful in the treatment, prevention and suppression of diseases mediated by the CB1 receptor. The compds. of the present invention are useful as centrally acting drugs in the treatment of psychosis, memory deficits, cognitive disorders, migraine, neuropathy, neuro-inflammatory disorders including multiple sclerosis and Guillain-Barre syndrome and the inflammatory sequelae of viral encephalitis, cerebral vascular accidents, and head trauma, anxiety disorders, stress, epilepsy, Parkinson's disease, movement disorders, and **schizophrenia**. The compds. are also useful for the treatment of substance abuse disorders, the treatment of obesity or eating disorders, as well as the treatment of asthma, constipation, chronic intestinal pseudo-obstruction, and cirrhosis of the liver. Although the methods of preparation are not claimed, more than 120 example prepns. of intermediates and >480 example prepns./characterization data for a library of I are included. For I: R1 = C1-10-alkyl, C3-10cycloalkyl, C3-10-cycloalkyl-C1-4-alkyl, cycloheteroalkyl, cycloheteroalkyl-C1-4alkyl, aryl, aryl-C1-4-alkyl, heteroaryl, heteroaryl-C1-4-alkyl, -ORd, -NRcRd, -NRcC(O)Rd, -CO2Rd, and -C(O)NRcRd. R2 = C1-10alkyl, C3-10cycloalkyl-C1-4alkyl, cycloheteroalkyl, cycloheteroalkyl-C1-4alkyl, aryl, aryl-C1-4alkyl, aryloxy, arylthio, heteroaryl, and heteroaryl-C1-4alkyl; R3 = H, and C1-4alkyl; R4 = H, and C1-4alkyl; R5 = C1-10alkyl, C2-10alkenyl, C3-10-cycloalkyl-C1-4alkyl, cycloheteroalkyl-C1-4-alkyl, aryl-C1-4-alkyl, diaryl-C1-4alkyl, aryl-C1-4alkenyl, heteroaryl-C1-4alkyl, -ORd, and -NRcRd; addnl. details including provisos are given in the claims.

ST amide prepn cannabinoid 1 receptor modulator therapy; antagonist cannabinoid 1 receptor amide prepn; inverse agonist cannabinoid 1 receptor amide prepn

IT Nervous system, disease
(Guillain-Barre syndrome; preparation of substituted amides as antagonists and/or inverse agonists of cannabinoid-1 receptor for therapy)

IT Drugs of abuse
(abuse of; preparation of substituted amides as antagonists and/or inverse agonists of cannabinoid-1 receptor for therapy)

IT Appetite
(bulimia; preparation of substituted amides as antagonists and/or inverse

605681-86-5P, Ethyl 2-[(6-Methyl-3-pyridyl)oxy]-2-methylpropionate
605685-08-3P, Benzyl 2(R)-[(5-Trifluoromethylpyridin-2-yl)oxy]propionate
606124-10-1P, (2R*,3R*)-2-Amino-3,4-diphenylbutane hydrochloride
606124-11-2P, (2R*,3S*)-2-Amino-3,4-diphenylbutane hydrochloride
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of substituted amides as antagonists and/or inverse agonists of cannabinoid-1 receptor for therapy)

L28 ANSWER 7 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:678507 CAPLUS
DOCUMENT NUMBER: 139:214467
TITLE: Preparation of 2-(**piperazinylmethyl**)-1H-benzimidazoles and related compounds that are useful in treating sexual dysfunction
INVENTOR(S): Cowart, Marlon D.; Bhatia, Pramila A.; Daanen, Jerome F.; Stewart, Andrew O.; Patel, Meena V.; Kolasa, Teodozyj; Brioni, Jorge D.; Rohde, Jeffrey; Engstrom, Kenneth M.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 53 pp., Cont.-in-part of U.S. Ser. No. 94,265.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003162790	A1	20030828	US 2002-236812	20020906
US 2002169167	A1	20021114	US 2002-94265	20020308
WO 2003076431	A1	20030918	WO 2003-US6406	20030304
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
BR 2003005708	A	20040928	BR 2003-5708	20030304
EP 1483258	A1	20041208	EP 2003-716268	20030304
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				

PRIORITY APPLN. INFO.:

US 2001-274805P	P	20010309
US 2001-296078P	P	20010605
US 2002-94265	A2	20020308
US 2001-340452P	P	20011214
US 2002-236812	A	20020906
WO 2003-US6406	W	20030304

OTHER SOURCE(S): MARPAT 139:214467
AN 2003:678507 CAPLUS
DN 139:214467
ED Entered STN: 29 Aug 2003
TI Preparation of 2-(**piperazinylmethyl**)-1H-benzimidazoles and related compounds that are useful in treating sexual dysfunction
IN Cowart, Marlon D.; Bhatia, Pramila A.; Daanen, Jerome F.; Stewart, Andrew O.; Patel, Meena V.; Kolasa, Teodozyj; Brioni, Jorge D.; Rohde, Jeffrey; Engstrom, Kenneth M.
PA USA

SO U.S. Pat. Appl. Publ., 53 pp., Cont.-in-part of U.S. Ser. No. 94,265.
CODEN: USXXCO
DT Patent
LA English
IC ICM A61K031-496
ICS A61K031-506; A61K031-4545; A61K031-454
NCL 514252190; 514253090; 514254040; 514254060; 514256000; 514322000
CC 28-9 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1
FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2003162790	A1	20030828	US 2002-236812	20020906
US 2002169167	A1	20021114	US 2002-94265	20020308
WO 2003076431	A1	20030918	WO 2003-US6406	20030304
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW				
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BR 2003005708	A	20040928	BR 2003-5708	20030304
EP 1483258	A1	20041208	EP 2003-716268	20030304
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
PRAI US 2001-274805P	P	20010309		
US 2001-296078P	P	20010605		
US 2002-94265	A2	20020308		
US 2001-340452P	P	20011214		
US 2002-236812	A	20020906		
WO 2003-US6406	W	20030304		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
US 2003162790	ICM	A61K031-496
	ICS	A61K031-506; A61K031-4545; A61K031-454
	NCL	514252190; 514253090; 514254040; 514254060; 514256000; 514322000

OS MARPAT 139:214467
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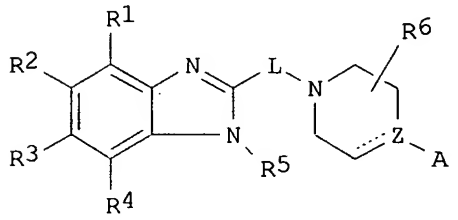

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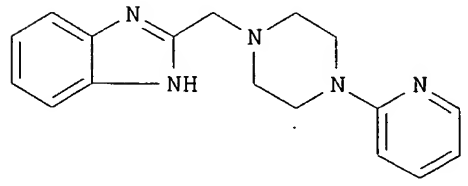

II

AB Title compds. (I) [wherein A = (un)substituted Ph, pyridinyl, pyrimidinyl, thienyl, pyrrolyl, furyl, imidazolyl, pyrazolyl, (is)oxazolyl, (iso)thiazolyl, triazolyl, tetrazolyl, etc.; L = CH2, CH2CH2, CH2CH2CH2, or CH2CH2CH2CH2; R1-R4 = independently H, alkoxy(carbonyl), alkenyl, (halo)alkyl, alkylthio, alkylsulfinyl, alkylsulfonyl, alkynyl, alkylcarbonyl(oxy), CO2H, CN, CHO, halo(alkoxy), OH, hydroxyalkyl, SH, NO2, or (un)substituted amino or carbamoyl; R5 = H, alkoxycarbonyl, alkyl, (cyclo)alkylcarbonyl, arylcarbonyl, heterocyclylcarbonyl, or (un)substituted carbamoyl; R6 = H or alkyl; Z = N, C, or CH; or pharmaceutically acceptable salt, ester, amide, or prodrug thereof] were prepared as dopamine agonists (no data) for the treatment of sexual dysfunction. For example, 2-chloromethylbenzimidazole and TEA were added to 1-(2-pyridyl)**piperazine** in DMF and the solution stirred at 20° for 16 h to give 2-[(4-pyridin-2-**ylpiperazin** -1-yl)methyl]-1H-benzimidazole (II) in 72% yield. The latter induced penile erection in Wistar rats with an incidence of 83% at a dose of 0.03 μmol/kg without inducing emesis.

ST **piperazinylmethyl** benzimidazole prepn sexual dysfunction dopamine agonist; piperidinylmethyl benzimidazole prepn sexual dysfunction dopamine agonist

IT Drugs of abuse
(abuse of; preparation of (heterocyclylalkyl)benzimidazole dopamine agonists for treatment of sexual dysfunction and other dopamine related disorders)

IT Mental disorder
(attention deficit hyperactivity disorder; preparation of (heterocyclylalkyl)benzimidazole dopamine agonists for treatment of sexual dysfunction and other dopamine related disorders)

IT Adrenoceptor antagonists
Dopamine agonists
(coadministration; preparation of (heterocyclylalkyl)benzimidazole dopamine agonists for treatment of sexual dysfunction and other dopamine related disorders)

IT Mental disorder
(depression; preparation of (heterocyclylalkyl)benzimidazole dopamine agonists for treatment of sexual dysfunction and other dopamine related disorders)

IT Sexual behavior
(disorder, female; preparation of (heterocyclylalkyl)benzimidazole dopamine agonists for treatment of sexual dysfunction and other dopamine related disorders)

IT Sexual behavior
(impotence; preparation of (heterocyclylalkyl)benzimidazole dopamine agonists for treatment of sexual dysfunction and other dopamine related disorders)

IT Mental disorder
(mood-affecting; preparation of (heterocyclylalkyl)benzimidazole dopamine agonists for treatment of sexual dysfunction and other dopamine related disorders)

IT Alzheimer's disease
Anti-Alzheimer's agents
Anti-inflammatory agents
Antidepressants
Antiparkinsonian agents
Antipsychotics
Anxiety
Anxiolytics
Cardiovascular agents
Cardiovascular system, disease
Dopamine agonists
Human

Inflammation
Parkinson's disease
Schizophrenia
(preparation of (heterocyclylalkyl)benzimidazole dopamine agonists for treatment of sexual dysfunction and other dopamine related disorders)

IT Drug delivery systems
(prodrugs; preparation of (heterocyclylalkyl)benzimidazole dopamine agonists for treatment of sexual dysfunction and other dopamine related disorders)

IT 70006-24-5P, 2-[[4-(Pyridin-2-yl)**piperazin**-1-yl]methyl]-1H-benzimidazole
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(dopamine agonist; preparation of (heterocyclylalkyl)benzimidazoles from heterocycles and (haloalkyl)benzimidazoles for treatment of sexual dysfunction)

IT 70006-20-1P, 2-[(4-**Phenylpiperazin**-1-yl)methyl]-1H-benzimidazole 70006-22-3P, 2-[[4-(2-Methoxyphenyl)**piperazin**-1-yl]methyl]-1H-benzimidazole 70006-25-6P, 2-[[4-(**1,3-Thiazol**-2-yl)**piperazin**-1-yl]methyl]-1H-benzimidazole 159557-22-9P, 2-[(4-Phenyl-3,6-dihydropyridin-1(2H)-yl)methyl]-1H-benzimidazole 474417-17-9P, 2-[[4-(Pyridin-2-yl)**piperazin**-1-yl]methyl]-1H-benzimidazole maleate (1:1) 474417-18-0P, 2-[[4-(Pyrimidin-2-yl)**piperazin**-1-yl]methyl]-1H-benzimidazole 474417-19-1P, 2-[[4-(6-Methylpyridin-2-yl)**piperazin**-1-yl]methyl]-1H-benzimidazole 474417-20-4P, 2-[4-[(1H-Benzimidazol-2-yl)methyl]**piperazin**-1-yl]nicotinonitrile 474417-21-5P, 5,7-Dibromo-2-[[4-(pyridin-2-yl)**piperazin**-1-yl]methyl]-1H-benzimidazole 474417-22-6P, 5-Fluoro-2-[[4-(pyridin-2-yl)**piperazin**-1-yl]methyl]-1H-benzimidazole 474417-24-8P, Isobutyl 2-[[4-(pyridin-2-yl)**piperazin**-1-yl]methyl]-1H-benzimidazole-1-carboxylate 474417-25-9P, 2-[[4-(Pyridin-2-yl)**piperazin**-1-yl]methyl]-1-(pyrrolidin-1-ylcarbonyl)-1H-benzimidazole 474417-26-0P, N,N-Dimethyl-2-[[4-(pyridin-2-yl)**piperazin**-1-yl]methyl]-1H-benzimidazole-1-carboxamide 474417-27-1P, 2-[4-[(1H-Benzimidazol-2-yl)methyl]**piperazin**-1-yl]benzonitrile 474417-28-2P, 2-[[4-(2-Chlorophenyl)**piperazin**-1-yl]methyl]-1H-benzimidazole 474417-29-3P, 2-[[4-(2-Fluorophenyl)**piperazin**-1-yl]methyl]-1H-benzimidazole 474417-30-6P, 2-[[4-(2-Nitrophenyl)**piperazin**-1-yl]methyl]-1H-benzimidazole 474417-31-7P, 2-[[4-(2-Nitrophenyl)**piperazin**-1-yl]methyl]-1H-benzimidazole trifluoroacetate (1:1) 474417-32-8P, 4-[4-[(1H-Benzimidazol-2-yl)methyl]**piperazin**-1-yl]phenol 474417-33-9P, 2-[[4-[2-(Methylthio)phenyl]**piperazin**-1-yl]methyl]-1H-benzimidazole 474417-34-0P, 2-[[4-(2-Ethoxyphenyl)**piperazin**-1-yl]methyl]-1H-benzimidazole 474417-35-1P, 2-[4-[(1H-Benzimidazol-2-yl)methyl]**piperazin**-1-yl]phenol 474417-36-2P, 2-[[4-(2-Methoxyphenyl)piperidin-1-yl]methyl]-1H-benzimidazole 474417-37-3P, 2-[(4-Pyridin-2-ylpiperidin-1-yl)methyl]-1H-benzimidazole 474417-39-5P, 2-[[2-Methyl-4-(pyridin-2-yl)**piperazin**-1-yl]methyl]-1H-benzimidazole 474417-41-9P, 2-[[(2S)-2-Methyl-4-(pyridin-2-yl)**piperazin**-1-yl]methyl]-1H-benzimidazole 474417-43-1P, 2-[[(2R)-2-Methyl-4-(pyridin-2-yl)**piperazin**-1-yl]methyl]-1H-benzimidazole 474417-45-3P, N-[2-[4-[(1H-Benzimidazol-2-yl)methyl]**piperazin**-1-yl]pyridin-3-yl]methanesulfonamide 474417-47-5P, 2-[[4-(3-Fluoropyridin-2-yl)**piperazin**-1-yl]methyl]-1H-benzimidazole 474417-48-6P, 6-[4-[(1H-Benzimidazol-2-yl)methyl]**piperazin**-1-yl]pyridin-3-ol 474417-51-1P, 2-[[4-(3-Methylpyridin-2-yl)**piperazin**-1-yl]methyl]-1H-benzimidazole 474417-52-2P, 2-[[4-(Pyridin-2-yl)**piperazin**-1-yl]methyl]-1H-benzimidazole bis((L)tartrate)
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU

(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(dopamine agonist; preparation of (heterocyclylalkyl)benzimidazoles from heterocycles and (haloalkyl)benzimidazoles for treatment of sexual dysfunction)

IT 9068-52-4, Phosphodiesterase 5
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitor, coadministration; preparation of (heterocyclylalkyl)benzimidazole dopamine agonists for treatment of sexual dysfunction and other dopamine related disorders)

IT 17282-04-1P, 2-Chloro-3-fluoropyridine 30532-37-7P, 4-(Pyrid-2-yl)piperidine 42270-37-1P, 1-(2-Thiazolyl)**piperazine** 84611-43-8P, 5-(Benzyloxy)-2-chloropyridine 85386-84-1P, 1-(3-Fluoropyridin-2-yl)**piperazine** 156144-42-2P, 5-Fluoro-2-chloromethylbenzimidazole 158955-23-8P, N-(2-Chloropyridin-3-yl)methanesulfonamide 161610-16-8P, Benzyl 4-hydroxy-4-pyridin-2-ylpiperidine-1-carboxylate 474417-23-7P, 1-(2-Thiazolyl)-4-(tert-butoxycarbonyl)**piperazine** 474417-40-8P, 3-Methyl-1-(pyridin-2-yl)**piperazine** hydrobromide 474417-42-0P, (3S)-3-Methyl-1-pyridin-2-**ylpiperazine** 474417-44-2P, (3R)-3-Methyl-1-pyridin-2-**ylpiperazine** 474417-46-4P, N-(2-**Piperazin**-1-ylpyridin-3-yl)methanesulfonamide 474417-49-7P, tert-Butyl 4-[5-(benzyloxy)pyridin-2-yl]**piperazine**-1-carboxylate 474417-50-0P, 2-[[4-[5-(Benzyloxy)pyridin-2-yl]**piperazin**-1-yl]methyl]-1H-benzimidazole
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of (heterocyclylalkyl)benzimidazoles from heterocycles and (haloalkyl)benzimidazoles for treatment of sexual dysfunction)

IT 587870-74-4P 587870-75-5P 587870-76-6P 587870-77-7P 587870-78-8P
587870-79-9P 587870-80-2P 587870-81-3P 587870-82-4P 587870-83-5P
587870-84-6P 587870-85-7P 587870-86-8P 587870-87-9P 587870-88-0P
587870-89-1P 587870-90-4P 587870-91-5P 587870-92-6P 587870-93-7P
587870-94-8P 587870-95-9P 587870-96-0P 587870-97-1P 587870-98-2P
587870-99-3P 587871-00-9P 587871-01-0P 587871-02-1P 587871-03-2P
587871-04-3P 587871-05-4P 587871-06-5P 587871-07-6P 587871-08-7P
587871-09-8P 587871-10-1P 587871-11-2P 587871-12-3P 587871-13-4P
587871-14-5P 587871-15-6P 587871-16-7P 587871-17-8P 587871-18-9P
587871-19-0P 587871-20-3P 587871-21-4P 587871-22-5P 587871-23-6P
587871-24-7P 587871-25-8P 587871-27-0P 587871-29-2P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of (heterocyclylalkyl)benzimidazoles from heterocycles and (haloalkyl)benzimidazoles for treatment of sexual dysfunction)

IT 79-44-7, N,N-Dimethylcarbamoyl chloride 92-54-6, 1-**Phenylpiperazine** 100-39-0, Benzyl bromide 109-04-6, 2-Bromopyridine 109-07-9, 2-**Methylpiperazine** 110-85-0, **Piperazine**, reactions 367-31-7, 4-Fluoro-1,2-phenylenediamine 372-47-4, 3-Fluoropyridine 543-27-1, Isobutyl chloroformate 1011-15-0, 1-(2-Fluorophenyl)**piperazine** 1011-17-2, 1-(2-Hydroxyphenyl)**piperazine** 1013-24-7, 1-(2-Methylthiophenyl)**piperazine** 1192-63-8, 1-Pyrrolidinecarbonyl chloride 1575-38-8, 4,6-Dibromo-1,2-phenylenediamine 3034-53-5, 2-Bromothiazole 4857-04-9, 2-Chloromethylbenzimidazole 4857-06-1, 2-Chlorobenzimidazole 6298-19-7, 2-Chloropyridin-3-ylamine 13339-01-0, 1-(2-Ethoxyphenyl)**piperazine** 19099-93-5, Benzyl 4-oxo-1-piperidine carboxylate 20980-22-7, 1-(2-Pyrimidyl)**piperazine** 34803-66-2, 1-(2-Pyridyl)**piperazine** 35386-24-4, 1-(2-Methoxyphenyl)**piperazine** 39512-50-0, 1-(2-Chlorophenyl)**piperazine** 41288-96-4, 2-Chloro-5-hydroxypyridine 43064-12-6, 4-Phenyl-1,2,3,6-tetrahydropyridine hydrochloride 55745-89-6, 1-(6-Methylpyridin-2-yl)

piperazine 56621-48-8, 1-(4-Hydroxyphenyl)**piperazine** 57260-71-6, tert-Butyl 1-**piperazinecarboxylate** 58333-75-8, 4-(2-Methoxyphenyl)piperidine 59084-06-9, 1-(2-Nitrophenyl)**piperazine** 74879-18-8, (S)-2-**Methylpiperazine** 75336-86-6, (R)-2-**Methylpiperazine** 84951-44-0, 1-(3-Cyanopyridin-2-yl)**piperazine** 111373-03-6, 1-(2-Cyanophenyl)**piperazine**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of (heterocyclylalkyl)benzimidazoles from heterocycles and (haloalkyl)benzimidazoles for treatment of sexual dysfunction)

L28 ANSWER 8 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:282556 CAPLUS
DOCUMENT NUMBER: 138:304161
TITLE: Preparation of 2-(aminoalkyl)chromans as 5-hydroxytryptamine-6 ligands for treatment of CNS disorders
INVENTOR(S): Greenblatt, Lynne Padilla; Kelly, Michael Gerard
PATENT ASSIGNEE(S): Wyeth, John, and Brother Ltd., USA
SOURCE: PCT Int. Appl., 63 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2003029238	A1	20030410	WO 2002-US30955		20020930
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW					
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EP 1432696	A1	20040630	EP 2002-800383		20020930
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BR 2002013094	A	20041013	BR 2002-13094		20020930
US 2003158175	A1	20030821	US 2002-263890		20021002
US 6706757	B2	20040316			
PRIORITY APPLN. INFO.:			US 2001-326957P	P	20011004
			WO 2002-US30955	W	20020930

OTHER SOURCE(S): MARPAT 138:304161
AN 2003:282556 CAPLUS
DN 138:304161
ED Entered STN: 11 Apr 2003
TI Preparation of 2-(aminoalkyl)chromans as 5-hydroxytryptamine-6 ligands for treatment of CNS disorders
IN Greenblatt, Lynne Padilla; Kelly, Michael Gerard
PA Wyeth, John, and Brother Ltd., USA
SO PCT Int. Appl., 63 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07D311-58
ICS C07D407-12; C07D405-12; C07D413-12; C07D409-12; C07D417-12; A61K031-35; C07D319-00; C07D311-00; C07D311-02; C07D213-00; C07D271-00

CC 27-14 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003029238	A1	20030410	WO 2002-US30955	20020930
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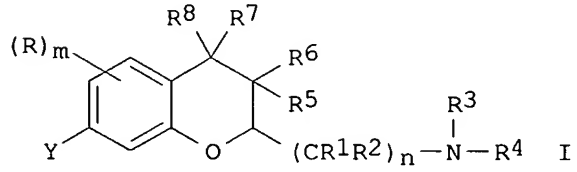
	US 6706757	B2	20040316		
PRAI	US 2001-326957P	P	20011004		
	WO 2002-US30955	W	20020930		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2003029238	ICM	C07D311-58
	ICS	C07D407-12; C07D405-12; C07D413-12; C07D409-12; C07D417-12; A61K031-35; C07D319-00; C07D311-00; C07D311-02; C07D213-00; C07D271-00
US 2003158175	ECLA	A61K031/353; C07D311/58; C07D405/12+311C+213; C07D407/12+317+311C; C07D409/12+333B+311C; C07D040/12+333+311C; C07D413/12+271+311C; C07D417/12+311C+277; C07D513/04+275C+235C

OS MARPAT 138:304161
GI



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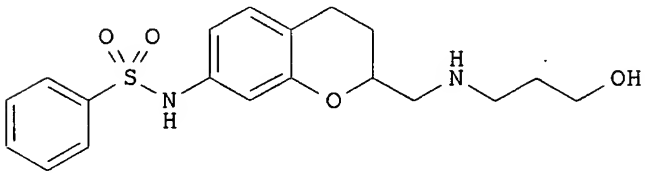

II

AB Title compds. I [wherein Y = SO2NR9R10 or NR11ZR12; Z = SO2, CONH, or CSNH; R = halo, CN, OR13, CO2R14, CONR15R16, SOxR17, or (un)substituted alkyl, alkenyl, alkynyl, cyclo(hetero)aryl, Ph, or heteroaryl; R1, R2, R5, R6, R7, R8, and R11 = independently H or (un)substituted alkyl; R3 and R4 = independently H or (un)substituted alkyl or (hetero)cycloalkyl; or NR3R4 = (un)substituted heterocyclyl; m = 0-3; n = 1-4; x = 0-2; R9 and R10 = independently H or (un)substituted alkyl or (hetero)aryl; R12 and R17 =

independently (un)substituted alkyl or (hetero)aryl; R13 = H, CO2R18, or (un)substituted alkyl, alkenyl, alkynyl, or (hetero)aryl; R14 and R18 = independently H or (un)substituted alkyl, alkenyl, alkynyl, cyclo(hetero)alkyl, or (hetero)aryl; R15 and R16 = independently H or (un)substituted alkyl; or stereoisomers or pharmaceutically acceptable salts thereof] were prepared as 5-hydroxytryptamine-6 (5-HT6) ligands. For example, cycloaddn. of N-(4-acetyl-3-hydroxyphenyl)acetamide with di-Et oxalate in the presence of NaOEt in EtOH provided Et 7-amino-4-oxo-4H-chromene-2-carboxylate (61%). Hydrogenation of the chroman (89%) with Pd/C, followed by reduction of the ester using LiBH4 gave 7-amino-2-(hydroxymethyl)chroman (90%). Addition of PhSO2Cl in pyridine afforded the N,O-disubstituted derivative (92%). Reaction with 3-amino-1-propanol in pyridine and conversion to the salt provided II•hemifumarate. The latter exhibited binding to the 5-HT6 receptor with Ki of 5 nM in cultured HeLa cells expressing human cloned 5-HT6 receptors. Thus, I are useful for the treatment of CNS disorders, such as motor disorder, anxiety, cognitive disorder, **schizophrenia**, depression, Alzheimer's disease, Parkinson's disease, and attention deficit disorder (no data).

ST aminoalkyl chroman prepn 5HT6 hydroxytryptamine receptor modulator CNS agent

IT 5-HT agonists
5-HT antagonists
(5-HT6; preparation of (aminoalkyl)chroman 5-HT6 ligands for treatment of CNS disorders)

IT Mental disorder
(attention deficit disorder; preparation of (aminoalkyl)chroman 5-HT6 ligands for treatment of CNS disorders)

IT Nervous system
(central; preparation of (aminoalkyl)chroman 5-HT6 ligands for treatment of CNS disorders)

IT Mental disorder
(cognitive; preparation of (aminoalkyl)chroman 5-HT6 ligands for treatment of CNS disorders)

IT Mental disorder
(depression; preparation of (aminoalkyl)chroman 5-HT6 ligands for treatment of CNS disorders)

IT Cognition
(disorder; preparation of (aminoalkyl)chroman 5-HT6 ligands for treatment of CNS disorders)

IT Behavior
(motor, disorder; preparation of (aminoalkyl)chroman 5-HT6 ligands for treatment of CNS disorders)

IT Alzheimer's disease
Anti-Alzheimer's agents
Antidepressants
Antiparkinsonian agents
Antipsychotics
Anxiety
Anxiolytics
Cognition enhancers
Human
Nervous system agents
Parkinson's disease
Schizophrenia
(preparation of (aminoalkyl)chroman 5-HT6 ligands for treatment of CNS disorders)

IT 5-HT receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(type 5-HT6; preparation of (aminoalkyl)chroman 5-HT6 ligands for treatment of CNS disorders)

IT 507277-05-6P, N-[(2R)-2-[[((1R)-1-Phenylethyl)amino]methyl]-3,4-dihydro-2H-chromen-7-yl]benzenesulfonamide 507277-07-8P, N-[(2S)-2-[[((1R)-1-Phenylethyl)amino]methyl]-3,4-dihydro-2H-chromen-7-yl]benzenesulfonamide

2620-50-0, 1,3-Benzodioxol-5-ylmethylamine 2627-86-3, 1(S)-Phenylethylamine 2766-74-7, 5-Chlorothiophene-2-sulfonyl chloride 2888-06-4, 3-Chlorobenzenesulfonyl chloride 2905-25-1, 2-Bromobenzenesulfonyl chloride 2991-42-6, 4-Trifluoromethylbenzenesulfonyl chloride 3731-52-0, Pyridin-3-ylmethylamine 3731-53-1, Pyridin-4-ylmethylamine 3886-69-9, (1R)-1-Phenyl-1-ethanamine 5071-96-5, 3-Methoxybenzylamine 5913-13-3 7617-76-7, 3-Phenoxypropylamine 16499-88-0, 3-Butoxypropylamine 22374-89-6, 1-Methyl-3-phenylpropylamine 23095-31-0, 3,4-Dimethoxybenzenesulfonyl chloride 24939-24-0, 4-Aminobenzenesulfonyl chloride 25611-78-3, 1,2-Diphenylethanamine 34698-41-4, 2,3-Dihydro-1H-inden-1-amine 40547-58-8, N-(4-Acetyl-3-hydroxyphenyl)acetamide 53448-09-2 55854-46-1, 5-Bromo-2-thiophenesulfonyl chloride 56613-80-0 69812-29-9 94108-56-2, 4-Trifluoromethoxybenzenesulfonyl chloride 114322-14-4, 2,1,3-Benzoxadiazole-4-sulfonyl chloride 150020-64-7 166964-33-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of (aminoalkyl)chroman 5-HT6 ligands for treatment of CNS disorders)

RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Bayer Ag; WO 9932475 A 1999 CAPLUS
(2) Boess, F; MOLECULAR PHARMACOLOGY 1998, V54, P577 CAPLUS
(3) Mewshaw, R; US 5663194 A 1997 CAPLUS
(4) Mewshaw, R; JOURNAL OF MEDICINAL CHEMISTRY 1997, V40(26), P4235 CAPLUS

L28 ANSWER 9 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:23532 CAPLUS
DOCUMENT NUMBER: 138:89812
TITLE: Preparation of heteroalkyl-substituted benzimidazoles useful in treating sexual dysfunction
INVENTOR(S): Cowart, Marlon D.; Bhatia, Pramila A.; Daanen, Jerome F.; Stewart, Andrew O.; Patel, Meena V.; Kolasa, Teodozyj; Brioni, Jorge D.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 44 pp., Cont.-in-part of U.S. Ser. No. 803,537, abandoned.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003008878	A1	20030109	US 2001-874484	20010605
US 2002169166	A1	20021114	US 2001-17939	20011214
CA 2439943	AA	20021107	CA 2002-2439943	20020306
WO 2002088093	A1	20021107	WO 2002-US7791	20020306
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1373220	A1	20040102	EP 2002-731130	20020306
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NO 2003003959	A	20031110	NO 2003-3959	20030908
PRIORITY APPLN. INFO.:			US 2001-803537	B2 20010309

US 2001-874484	A2	20010605
US 2001-17939	A	20011214
WO 2002-US7791	W	20020306

OTHER SOURCE(S): MARPAT 138:89812
AN 2003:23532 CAPLUS
DN 138:89812
ED Entered STN: 10 Jan 2003
TI Preparation of heteroalkyl-substituted benzimidazoles useful in treating sexual dysfunction
IN Cowart, Marlon D.; Bhatia, Pramila A.; Daanen, Jerome F.; Stewart, Andrew O.; Patel, Meena V.; Kolasa, Teodozyj; Brioni, Jorge D.
PA USA
SO U.S. Pat. Appl. Publ., 44 pp., Cont.-in-part of U.S. Ser. No. 803,537, abandoned.
CODEN: USXXCO
DT Patent
LA English
IC ICM A61K031-496
NCL 514252190; 514254060; 514254040; 514254030; 514253090
CC 28-9 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 63
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2003008878	A1	20030109	US 2001-874484	20010605
	US 2002169166	A1	20021114	US 2001-17939	20011214
	CA 2439943	AA	20021107	CA 2002-2439943	20020306
	WO 2002088093	A1	20021107	WO 2002-US7791	20020306
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	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
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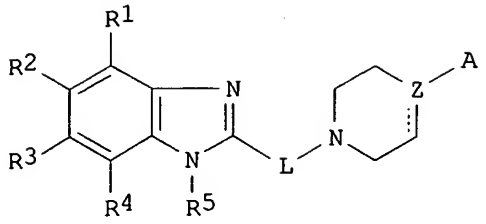
	NO 2003003959	A	20031110	NO 2003-3959	20030908
PRAI	US 2001-803537	B2	20010309		
	US 2001-874484	A2	20010605		
	US 2001-17939	A	20011214		
	WO 2002-US7791	W	20020306		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
US 2003008878	ICM	A61K031-496
	NCL	514252190; 514254060; 514254040; 514254030; 514253090

OS MARPAT 138:89812
GI



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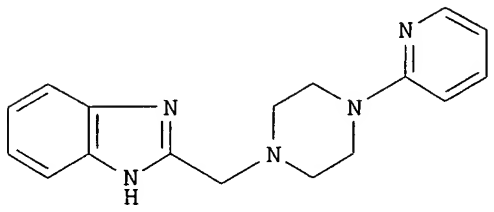

II

AB Title compds. I [A = (hetero)aryl; L = CH2, CH2CH2, etc.; R1-4 = H, alkoxy, alkenyl, alkyl, alkylsulfinyl, alkylsulfonyl, etc.; R5 = H, alkoxycarbonyl, alkyl, etc.; Z = N, C(H)] are prepared For instance, 1-(2-pyridyl)**piperazine** is alkylated with 2-chloromethylbenzimidazole (DMF, Et3N, 16 h) to give II. II induced statistically significant penile erections in rats after s.c. administration for doses of 0.01 μmol/kg to 0.10 μmol/kg. I are useful for the treatment of sexual dysfunction.

ST benzimidazole sexual dysfunction dopamine agonists prepn

IT Drugs of abuse
(abuse of; heteroalkyl-substituted benzimidazoles as dopamine agonists useful in treating sexual dysfunction)

IT Mental disorder
(attention deficit hyperactivity disorder; heteroalkyl-substituted benzimidazoles as dopamine agonists useful in treating sexual dysfunction)

IT Mental disorder
(depression; heteroalkyl-substituted benzimidazoles as dopamine agonists useful in treating sexual dysfunction)

IT Sexual behavior
(disorder; heteroalkyl-substituted benzimidazoles as dopamine agonists useful in treating sexual dysfunction)

IT Adrenoceptor antagonists
Alzheimer's disease
Anti-Alzheimer's agents
Anti-inflammatory agents
Antidepressants
Antiparkinsonian agents
Anxiety
Anxiolytics
Cardiovascular system, disease
Human
Parkinson's disease
Schizophrenia
Vomiting
(heteroalkyl-substituted benzimidazoles as dopamine agonists useful in treating sexual dysfunction)

IT Mental disorder
(mood-affecting; heteroalkyl-substituted benzimidazoles as dopamine agonists useful in treating sexual dysfunction)

IT Sexual behavior

59084-06-9, 1-(2-Nitrophenyl)**piperazine** 84951-44-0,
1-(3-Cyanopyridin-2-yl)**piperazine** 104396-10-3,
1-(3-Methylpyridin-2-yl)**piperazine** 108662-49-3,
5-Fluoro-2-chlorobenzimidazole 111373-03-6, 1-(2-Cyanophenyl)
piperazine
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of heteroalkyl-substituted benzimidazoles as dopamine agonists useful in treating sexual dysfunction)

IT 30532-37-7P, 4-(Pyridin-2-yl)piperidine 156144-42-2P,
5-Fluoro-2-chloromethylbenzimidazole 161610-16-8P, Benzyl
4-hydroxy-4-(pyridin-2-yl)piperidine-1-carboxylate 474417-23-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of heteroalkyl-substituted benzimidazoles as dopamine agonists useful in treating sexual dysfunction)

L28 ANSWER 10 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:869583 CAPLUS
DOCUMENT NUMBER: 137:353027
TITLE: Preparation of 2-(**piperazinylmethyl**)-1H-benzimidazoles and related compounds that are useful in treating sexual dysfunction
INVENTOR(S): Cowart, Marlon D.; Bhatia, Pramila A.; Daanen, Jerome F.; Stewart, Andrew O.; Patel, Meena V.; Kolasa, Teodozyj; Brioni, Jorge D.; Rohde, Jeffrey
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 53 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2002169167	A1	20021114	US 2002-94265		20020308
US 2003162790	A1	20030828	US 2002-236812		20020906
WO 2003076431	A1	20030918	WO 2003-US6406		20030304
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
BR 2003005708	A	20040928	BR 2003-5708		20030304
EP 1483258	A1	20041208	EP 2003-716268		20030304
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US 2004110766	A1	20040610	US 2003-699465		20031031
PRIORITY APPLN. INFO.:			US 2001-274805P	P	20010309
			US 2001-296078P	P	20010605
			US 2001-340452P	P	20011214
			US 2002-94265	A2	20020308
			US 2002-236812	A	20020906
			WO 2003-US6406	W	20030304

OTHER SOURCE(S): MARPAT 137:353027
AN 2002:869583 CAPLUS
DN 137:353027
ED Entered STN: 15 Nov 2002

1-(2-Cyanophenyl)**piperazine**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of (heterocyclylalkyl)benzimidazoles from heterocycles and (haloalkyl)benzimidazoles for treatment of sexual dysfunction)

L28 ANSWER 11 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:869582 CAPLUS
DOCUMENT NUMBER: 137:353026
TITLE: Preparation of 2-(**piperazinylmethyl**)-1H-benzimidazoles and related compounds that are useful in treating sexual dysfunction
INVENTOR(S): Cowart, Marlon D.; Bhatia, Pramila A.; Daanen, Jerome F.; Stewart, Andrew O.; Patel, Meena V.; Kolasa, Teodozyj; Brioni, Jorge D.; Rohde, Jeffrey
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 53 pp., Cont.-in-part of U.S. Ser. No. 874,484.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002169166	A1	20021114	US 2001-17939	20011214
US 2003008878	A1	20030109	US 2001-874484	20010605
CA 2439943	AA	20021107	CA 2002-2439943	20020306
WO 2002088093	A1	20021107	WO 2002-US7791	20020306
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1373220	A1	20040102	EP 2002-731130	20020306
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
NO 2003003959	A	20031110	NO 2003-3959	20030908
PRIORITY APPLN. INFO.:			US 2001-803537 B2	20010309
			US 2001-874484 A2	20010605
			US 2001-17939 A	20011214
			WO 2002-US7791 W	20020306

OTHER SOURCE(S): MARPAT 137:353026
AN 2002:869582 CAPLUS
DN 137:353026
ED Entered STN: 15 Nov 2002
TI Preparation of 2-(**piperazinylmethyl**)-1H-benzimidazoles and related compounds that are useful in treating sexual dysfunction
IN Cowart, Marlon D.; Bhatia, Pramila A.; Daanen, Jerome F.; Stewart, Andrew O.; Patel, Meena V.; Kolasa, Teodozyj; Brioni, Jorge D.; Rohde, Jeffrey
PA USA
SO U.S. Pat. Appl. Publ., 53 pp., Cont.-in-part of U.S. Ser. No. 874,484.
CODEN: USXXCO
DT Patent
LA English
IC ICM A61K031-496
NCL 514252190
CC 28-9 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1

FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2002169166	A1	20021114	US 2001-17939	20011214
	US 2003008878	A1	20030109	US 2001-874484	20010605
	CA 2439943	AA	20021107	CA 2002-2439943	20020306
	WO 2002088093	A1	20021107	WO 2002-US7791	20020306
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	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	EP 1373220	A1	20040102	EP 2002-731130	20020306
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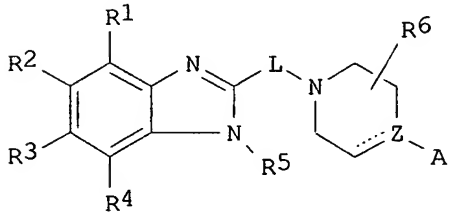
PRAI	US 2001-803537	B2	20010309		
	US 2001-874484	A2	20010605		
	US 2001-17939	A	20011214		
	WO 2002-US7791	W	20020306		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
US 2002169166	ICM	A61K031-496
	NCL	514252190

OS MARPAT 137:353026

GI



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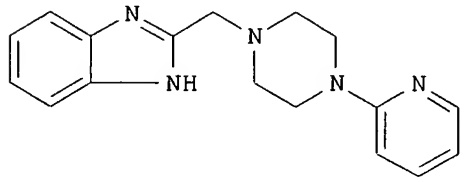


II

AB Title compds. (I) [wherein A = (un)substituted Ph, pyridinyl, pyrimidinyl, thienyl, pyrrolyl, furyl, imidazolyl, pyrazolyl, (is)oxazolyl, (iso)thiazolyl, triazolyl, tetrazolyl, etc.; L = CH2, CH2CH2, CH2CH2CH2, or CH2CH2CH2CH2; R1-R4 = independently H, alkoxy(carbonyl), alkenyl, (halo)alkyl, alkylthio, alkylsulfinyl, alkylsulfonyl, alkynyl, alkylcarbonyl(oxy), CO2H, CN, CHO, halo(alkoxy), OH, hydroxyalkyl, SH, NO2, or (un)substituted amino or carbamoyl; R5 = H, alkoxycarbonyl, alkyl, (cyclo)alkylcarbonyl, arylcarbonyl, heterocyclylcarbonyl, or (un)substituted carbamoyl; R6 = H or alkyl; Z = N, C, or CH; or pharmaceutically acceptable salt, ester, amide, or prodrug thereof] were prepared as dopamine agonists (no data) for the treatment of sexual

-1-ylpyridin-3-yl)methanesulfonamide 474417-49-7P, tert-Butyl 4-[5-(benzyloxy)pyridin-2-yl]**piperazine**-1-carboxylate 474417-50-0P, 2-[[4-[5-(Benzyloxy)pyridin-2-yl]**piperazin**-1-yl]methyl]-1H-benzimidazole
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of (heterocyclylalkyl)benzimidazoles from heterocycles and (haloalkyl)benzimidazoles for treatment of sexual dysfunction)

IT 79-44-7, N,N-Dimethylcarbamoyl chloride 92-54-6, 1-**Phenylpiperazine** 100-39-0, Benzyl bromide 109-04-6, 2-Bromopyridine 109-07-9, 2-**Methylpiperazine** 110-85-0, **Piperazine**, reactions 367-31-7, 4-Fluoro-1,2-phenylenediamine 372-47-4, 3-Fluoropyridine 543-27-1, Isobutyl chloroformate 1011-15-0, 1-(2-Fluorophenyl)**piperazine** 1011-17-2, 1-(2-Hydroxyphenyl)**piperazine** 1013-24-7, 1-(2-Methylthiophenyl)**piperazine** 1192-63-8, 1-Pyrrolidinecarbonyl chloride 1575-38-8, 4,6-Dibromo-1,2-phenylenediamine 3034-53-5, 2-Bromothiazole 4857-04-9, 2-Chloromethylbenzimidazole 4857-06-1, 2-Chlorobenzimidazole 6298-19-7, 2-Chloropyridin-3-ylamine 13339-01-0, 1-(2-Ethoxyphenyl)**piperazine** 19099-93-5, Benzyl 4-oxo-1-piperidine carboxylate 20980-22-7, 1-(2-Pyrimidyl)**piperazine** 34803-66-2, 1-(2-Pyridyl)**piperazine** 35386-24-4, 1-(2-Methoxyphenyl)**piperazine** 39512-50-0, 1-(2-Chlorophenyl)**piperazine** 41288-96-4, 2-Chloro-5-hydroxypyridine 43064-12-6, 4-Phenyl-1,2,3,6-tetrahydropyridine hydrochloride 55745-89-6, 1-(6-Methylpyridin-2-yl)**piperazine** 56621-48-8, 1-(4-Hydroxyphenyl)**piperazine** 57260-71-6, tert-Butyl 1-**piperazinecarboxylate** 58333-75-8, 4-(2-Methoxyphenyl)piperidine 59084-06-9, 1-(2-Nitrophenyl)**piperazine** 74879-18-8, (S)-2-**Methylpiperazine** 75336-86-6, (R)-2-**Methylpiperazine** 84951-44-0, 1-(3-Cyanopyridin-2-yl)**piperazine** 111373-03-6, 1-(2-Cyanophenyl)**piperazine**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of (heterocyclylalkyl)benzimidazoles from heterocycles and (haloalkyl)benzimidazoles for treatment of sexual dysfunction)

L28 ANSWER 12 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:849600 CAPLUS
DOCUMENT NUMBER: 137:353023
TITLE: Preparation of 2-heterocycloalkyl-benzimidazole derivatives for treating sexual dysfunction
INVENTOR(S): Cowart, Marlon D.; Bhatia, Pramila A.; Daanen, Jerome F.; Stewart, Andrew O.; Kolasa, Teodozyj; Rohde, Jeffrey J.; Patel, Meena V.; Brioni, Jorge D.
PATENT ASSIGNEE(S): Abbott Laboratories, USA
SOURCE: PCT Int. Appl., 115 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002088093	A1	20021107	WO 2002-US7791	20020306

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,

CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2003008878	A1	20030109	US 2001-874484		20010605
US 2002169166	A1	20021114	US 2001-17939		20011214
CA 2439943	AA	20021107	CA 2002-2439943		20020306
EP 1373220	A1	20040102	EP 2002-731130		20020306
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
NO 2003003959	A	20031110	NO 2003-3959		20030908
PRIORITY APPLN. INFO.:			US 2001-803537	A	20010309
			US 2001-874484	A	20010605
			US 2001-17939	A	20011214
			WO 2002-US7791	W	20020306

OTHER SOURCE(S): MARPAT 137:353023
AN 2002:849600 CAPLUS
DN 137:353023
ED Entered STN: 08 Nov 2002
TI Preparation of 2-heterocycloalkyl-benzimidazole derivatives for treating sexual dysfunction
IN Cowart, Marlon D.; Bhatia, Pramila A.; Daanen, Jerome F.; Stewart, Andrew O.; Kolasa, Teodozyj; Rohde, Jeffrey J.; Patel, Meena V.; Brioni, Jorge D.
PA Abbott Laboratories, USA
SO PCT Int. Appl., 115 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07D235-06
ICS A61P015-10; A61K031-4188
CC 28-9 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 63
FAN.CNT 3

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2002088093	A1	20021107	WO 2002-US7791	20020306
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003008878	A1	20030109	US 2001-874484	20010605
US 2002169166	A1	20021114	US 2001-17939	20011214
CA 2439943	AA	20021107	CA 2002-2439943	20020306
EP 1373220	A1	20040102	EP 2002-731130	20020306
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
NO 2003003959	A	20031110	NO 2003-3959	20030908
PRAI US 2001-803537	A	20010309		
US 2001-874484	A	20010605		
US 2001-17939	A	20011214		
WO 2002-US7791	W	20020306		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2002088093	ICM	C07D235-06
	ICS	A61P015-10; A61K031-4188

OS MARPAT 137:353023
GI

L28 ANSWER 13 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:814116 CAPLUS
DOCUMENT NUMBER: 137:325417
TITLE: Preparation and application of 5-membered heterocycles as medicaments
INVENTOR(S): Harnett, Jeremiah; Bigg, Dennis; Liberatore, Anne-Marie; Rolland, Alain
PATENT ASSIGNEE(S): Societe De Conseils De Recherches Et D'applications Scientifiques (SCRAS), Fr.
SOURCE: PCT Int. Appl., 132 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002083656	A2	20021024	WO 2002-FR1218	20020409
WO 2002083656	A3	20030103		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
FR 2823208	A1	20021011	FR 2001-4943	20010410
FR 2823208	B1	20040319		
CA 2443403	AA	20021024	CA 2002-2443403	20020409
EP 1379514	A2	20040114	EP 2002-761921	20020409
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004531526	T2	20041014	JP 2002-581412	20020409
NO 2003004524	A	20031029	NO 2003-4524	20031009

PRIORITY APPLN. INFO.:

FR 2001-4943	A	20010410
FR 2002-1811	A	20020214
WO 2002-FR1218	W	20020409

AN 2002:814116 CAPLUS
DN 137:325417
ED Entered STN: 25 Oct 2002
TI Preparation and application of 5-membered heterocycles as medicaments
IN Harnett, Jeremiah; Bigg, Dennis; Liberatore, Anne-Marie; Rolland, Alain
PA Societe De Conseils De Recherches Et D'applications Scientifiques (SCRAS), Fr.
SO PCT Int. Appl., 132 pp.
CODEN: PIXXD2
DT Patent
LA French
IC ICM C07D277-28
ICS A61K031-416; A61P043-00; C07D277-34; C07D417-04; C07D417-06; C07D233-50; C07D401-06; C07D417-14; C07D233-54
CC 28-9 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 7, 63
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002083656	A2	20021024	WO 2002-FR1218	20020409
	WO 2002083656	A3	20030103		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

FR	2823208	A1	20021011	FR 2001-4943	20010410
FR	2823208	B1	20040319		
CA	2443403	AA	20021024	CA 2002-2443403	20020409
EP	1379514	A2	20040114	EP 2002-761921	20020409

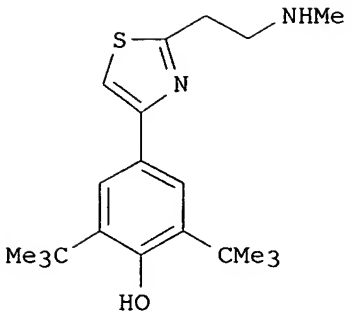
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

JP	2004531526	T2	20041014	JP 2002-581412	20020409
NO	2003004524	A	20031029	NO 2003-4524	20031009
PRAI FR	2001-4943	A	20010410		
FR	2002-1811	A	20020214		
WO	2002-FR1218	W	20020409		

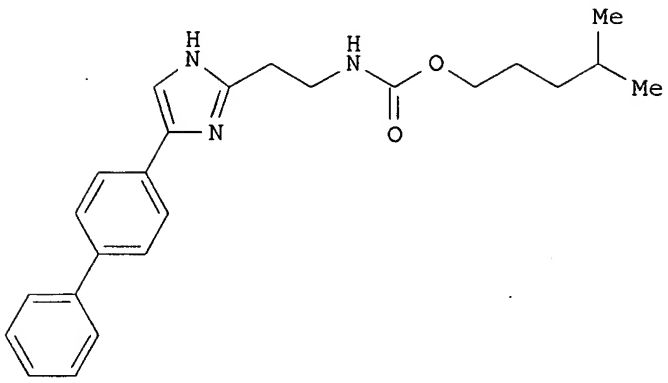
CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2002083656	ICM	C07D277-28
	ICS	A61K031-416; A61P043-00; C07D277-34; C07D417-04; C07D417-06; C07D233-50; C07D401-06; C07D417-14; C07D233-54
JP 2004531526	FTERM	4C033/AD03; 4C033/AD06; 4C033/AD17; 4C033/AD20; 4C056/AA01; 4C056/AB01; 4C056/AC02; 4C056/AD01; 4C056/AE03; 4C056/BA08; 4C056/BA11; 4C056/BB01; 4C056/BC01; 4C063/AA01; 4C063/AA03; 4C063/BB01; 4C063/BB03; 4C063/CC64; 4C063/DD10; 4C063/DD36; 4C063/DD62; 4C063/EE01; 4C086/AA02; 4C086/AA03; 4C086/BC38; 4C086/BC73; 4C086/BC82; 4C086/BC88; 4C086/GA07; 4C086/GA09; 4C086/GA10; 4C086/MA01; 4C086/MA04; 4C086/NA14; 4C086/ZA01; 4C086/ZA08; 4C086/ZA12; 4C086/ZA15; 4C086/ZA16; 4C086/ZA18; 4C086/ZA21; 4C086/ZC02

GI



I



II

AB The invention relates to thiazole, oxazole or imidazole derivs. having at least one of the following pharmacol. activities:: inhibition of monoamine oxydases (MAO); inhibition of lipid peroxidn.; modulation of sodium channels. The inventive compds. comprise, for example, 2,6-di(tert-butyl)-4-{2-[2-(methylamino)ethyl]-**1,3-thiazol**-4-yl}phenol (I); and 4-methylpentyl 2-[4-(1,1'-biphenyl-4-yl)-1H-imidazol-2-yl]ethyl carbamate (II). Thus, I·HCl was prepared from N-methyl-β-alaninenitrile via. N-protection with (Boc)2O in CH2Cl2 containing EtN(CHMe2)2, sulfurization with H2S in EtOH containing Et3N, cyclocondensation with α-bromo-1-[3,5-di(tert-butyl)-4-hydroxyphenyl]ethanone and acid-catalyzed deprotection with HCl in EtOAc. By virtue of their pharmacol. properties, said compds. can be used to treat one of the following disorders or diseases: Parkinson's disease, senile dementia, Alzheimer's disease, Huntington's chorea, amyotrophic lateral sclerosis, **schizophrenia**, depression, psychoses, migraine or pain, especially neuropathic pain. The pharmacol. activity of I was determined [CI50 ≤ 10 μM vs. monoamine oxydase B; CI50 ≤ 10 μM vs. lipid peroxidn.; CI50 ≤ 1.0 μM on sodium channels from the cerebral cortex of rats].

ST heterocycle prepn pharmacol activity application medicament; thiazole deriv prepn pharmacol activity application medicament; oxazole deriv prepn pharmacol activity application medicament; imidazole deriv prepn pharmacol activity application medicament; monoamine oxydase heterocycle inhibitor prepn; lipid peroxydation heterocycle inhibitor prepn; sodium channel heterocycle modulator prepn; thiazolylphenol methylaminoethyl deriv prepn pharmacol activity application medicament; imidazolylethylcarbamate methylpentyl deriv prepn pharmacol activity application medicament

IT Heterocyclic compounds
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(5-membered; preparation of 5-membered heterocycles with one of the following pharmacol. activities: monoamine oxydase inhibition, lipid peroxydation or sodium channel modulation)

alaninenitrile 2566-32-7, N-Methyl-DL-valine 13734-31-1, N-Boc-N-methyl-DL-alanine 14386-64-2, 2-Bromo-1-[3,5-di(tert-butyl)-4-hydroxyphenyl]ethan-1-one 93989-34-5, 2-Bromo-1-[10-(chloroacetyl)-10H-phenothiazin-2-yl]ethanone 175204-79-2, 2-(tert-Butylcarbonyloxy)thioacetamide
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of 5-membered heterocycles with one of the following pharmacol. activities: monoamine oxydase inhibition, lipid peroxydation or sodium channel modulation)

IT 3303-84-2P, N-Boc-β-alanine 5325-15-5P, 2-Chloro-1-(10H-phenothiazin-2-yl)ethanone 14035-34-8P, 1-[3,5-Di(tert-butyl)-4-hydroxyphenyl]propan-1-one 17055-13-9P, 2-Bromo-1-[3,5-di(tert-butyl)-4-hydroxyphenyl]propan-1-one 18621-17-5P, 1-(Diphenylmethyl)-3-hydroxyazetidine 23600-83-1P, 1-(4-Anilinophenyl)ethanone 49548-40-5P, Benzyl (2-amino-2-thioxoethyl) carbamate 73932-64-6P, 1-(1,1'-Biphenyl-4-yl)-2-bromo-1-propanone 92794-67-7P 101283-34-5P, N-(4-Acetylphenyl)-N-phenylacetamide 128304-84-7P, tert-Butyl N-(2-cyanoethyl)-N-methylcarbamate 136203-22-0P 206123-21-9P 218944-58-2P 218944-60-6P 335242-74-5P 335242-75-6P 335247-54-6P 335247-55-7P 335247-58-0P 347190-30-1P 473541-38-7P 473541-39-8P 473541-40-1P 473541-41-2P 473541-42-3P 473541-43-4P 473541-44-5P 473541-45-6P 473541-46-7P 473541-48-9P, 2-[2-(Bromomethyl)-1,3-thiazolyl]-10H-phenothiazine 473541-49-0P 473541-91-2P 473541-92-3P 473541-97-8P 473542-72-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 5-membered heterocycles with one of the following pharmacol. activities: monoamine oxydase inhibition, lipid peroxydation or sodium channel modulation)

IT 626-89-1, 4-Methyl-1-pentanol
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with triphosgene in; preparation of 5-membered heterocycles with one of the following pharmacol. activities: monoamine oxydase inhibition, lipid peroxydation or sodium channel modulation)

IT 70-23-5, Ethyl bromopyruvate
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction with heterocycle precursor in; preparation of 5-membered heterocycles with one of the following pharmacol. activities: monoamine oxydase inhibition, lipid peroxydation or sodium channel modulation)

IT 67-64-1, Acetone, reactions 110-62-3, Valeraldehyde 123-38-6, Propionaldehyde, reactions 630-19-3, Pivaldehyde
RL: RCT (Reactant); RACT (Reactant or reagent)
(reductive alkylation by, of heterocyclic intermediate; preparation of 5-membered heterocycles with one of the following pharmacol. activities: monoamine oxydase inhibition, lipid peroxydation or sodium channel modulation)

IT 108-94-1, Cyclohexanone, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(reductive amination of, in; preparation of 5-membered heterocycles with one of the following pharmacol. activities: monoamine oxydase inhibition, lipid peroxydation or sodium channel modulation)

IT 949-90-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(sulfurization of, in; preparation of 5-membered heterocycles with one of the following pharmacol. activities: monoamine oxydase inhibition, lipid peroxydation or sodium channel modulation)

IT 5325-64-4, Sarcosinamide hydrochloride
RL: RCT (Reactant); RACT (Reactant or reagent)
(tert-butoxycarbonylation of; preparation of 5-membered heterocycles with one of the following pharmacol. activities: monoamine oxydase inhibition, lipid peroxydation or sodium channel modulation)

L28 ANSWER 14 OF 21 CAPLUS

ACCESSION NUMBER: 2002:790220 CAPLUS
DOCUMENT NUMBER: 137:294982
TITLE: Preparation of piperazinylpyrazinyl aryloxyalkyl ethers as 5-HT2C receptor agonists
INVENTOR(S): Nilsson, Bjorn; Tejbrant, Jan; Pelcman, Benjamin; Ringberg, Erik; Thor, Markus; Nilsson, Jonas; Jonsson, Mattias
PATENT ASSIGNEE(S): Biovitrum AB, Swed.
SOURCE: U.S., 45 pp., Cont.-in-part of U.S. Ser. No. 573,348, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6465467	B1	20021015	US 2000-589282	20000608
ZA 2001009571	A	20021120	ZA 2001-9571	20011120
US 2003092694	A1	20030515	US 2002-269670	20021011
US 6759401	B2	20040706		
US 2004242554	A1	20041202	US 2004-873852	20040622

PRIORITY APPLN. INFO.:

SE 1999-1884	A	19990521
US 1999-137527P	P	19990603
US 2000-573348	B2	20000519
US 2000-589282	A3	20000608
US 2002-269670	A1	20021011

OTHER SOURCE(S): MARPAT 137:294982
AN 2002:790220 CAPLUS
DN 137:294982
ED Entered STN: 17 Oct 2002
TI Preparation of piperazinylpyrazinyl aryloxyalkyl ethers as 5-HT2C receptor agonists
IN Nilsson, Bjorn; Tejbrant, Jan; Pelcman, Benjamin; Ringberg, Erik; Thor, Markus; Nilsson, Jonas; Jonsson, Mattias
PA Biovitrum AB, Swed.
SO U.S., 45 pp., Cont.-in-part of U.S. Ser. No. 573,348, abandoned.
CODEN: USXXAM
DT Patent
LA English
IC ICM A61K031-495
ICS A61K031-4965; A61K031-50
NCL 514252110
CC 28-17 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6465467	B1	20021015	US 2000-589282	20000608
	ZA 2001009571	A	20021120	ZA 2001-9571	20011120
	US 2003092694	A1	20030515	US 2002-269670	20021011
	US 6759401	B2	20040706		
	US 2004242554	A1	20041202	US 2004-873852	20040622
PRAI	SE 1999-1884	A	19990521		
	US 1999-137527P	P	19990603		
	US 2000-573348	B2	20000519		
	US 2000-589282	A3	20000608		
	US 2002-269670	A1	20021011		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
US 6465467	ICM	A61K031-495

	ICS	A61K031-4965; A61K031-50
	NCL	514252110
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US 2003092694	ECLA	C07D241/18; C07D241/20; C07D401/12+241B+213; C07D403/12+241B+215; C07D403/12+241B+217; C07D; C07D403/12+241B+239; C07D403/12+309+241B; C07D405/12+307B+241B; C07D405/12+319+241; C07D413/12+263+241B; C07D417/12+277B+241B; C07D491/04+319B+221B

OS MARPAT 137:294982

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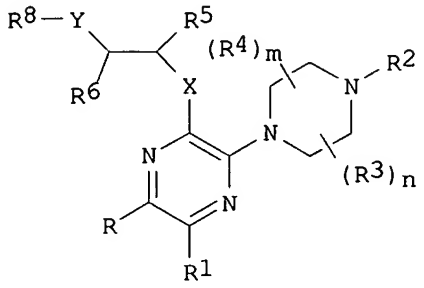

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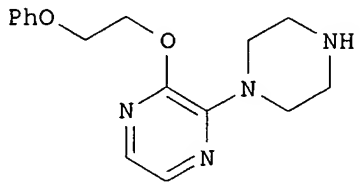

II

AB The title compds. (I) [wherein X and Y = independently O, S, or NR7; R and R1 = independently H, alkyl, or halo; or C2RR1 = optionally halo substituted benzene or thiophene; R2 = H, OH, or alkyl; R3, R4, and R5 = independently H or alkyl; R6 = H or alkyl; or CYR6R8 for a 5-6 membered heterocycle; R7 = H or alkyl, preferably Me or Et; R8 = (un)substituted (hetero)aryl; m and n = independently 1 or 2; or pharmaceutically acceptable salts, hydrates, geometric isomers, tautomers, optical isomers, N-oxides, and prodrugs thereof] were prepared and tested as 5-HT2C receptor agonists. For instance, 2,3-dichloropyrazine and 2-phenoxyethanol were treated with t-BuONa in dioxane to give 2-chloro-3-(2-phenoxyethoxy)pyrazine (62%). The halopyrazine, piperazine, and K2CO3 in MeCN were stirred and heated to afford the desired 2-(phenoxy)ethyl 3-(1-piperazinyl)-2-pyrazinyl ether (II) in 65% yield, which was then converted to the maleate salt. In competition expts., I showed affinity for 5-HT2C receptor protein with Ki values typically ranging from 1 nM to 1500 nM and specific values ranging from 5 nM to 377 nM for twelve compds. I exhibited agonist efficacy at the 5-HT2C receptor by mobilizing intracellular Ca in transfected HEK293 cells with maximum responses in the range of 20-100% relative to the maximum response of 5-HT (serotonin) at a concentration of 1 μM. Acute toxicity studies in mice following oral administration of I showed that mortality typically occurred at doses between 200 mg/kg to 450 mg/kg body weight I are useful for the treatment of serotonin-related central nervous system disorders, such as eating disorders, memory disorders, **schizophrenia**, mood disorders, anxiety disorders, pain, sexual dysfunctions, and urinary disorders (no data).

ST piperazinylpyrazinyl aryloxyalkyl ether prepn serotonin receptor agonist; aryloxyalkoxy piperazinyl pyrazine prepn central nervous system agent

IT Appetite
Memory, biological
Sexual behavior
(disorder; preparation of heterocyclylpyrazinyl aryloxyalkyl ether 5-HT2C

313657-79-3P, 2-[(2-Chloro-3-pyridinyl)oxy]ethanol 313657-88-4P, 2-[[2-(Methylsulfanyl)-3-pyridinyl]oxy]ethanol 313657-93-1P, 2-Bromo-3-[2-[[tert-butyldimethylsilyl]oxy]ethoxy]pyridine 313657-94-2P, 2-[(2-Ethoxy-3-pyridinyl)oxy]ethanol 313657-99-7P, 2-[(5-Ethoxy-3-pyridinyl)oxy]-1-ethanol 313658-02-5P, 2-[(6-Chloro-3-pyridinyl)oxy]-1-ethanol 313658-07-0P, 2-[(6-Methoxy-3-pyridinyl)oxy]-1-ethanol 313658-10-5P, 2-[5-(Dimethylamino)-2-methoxyphenoxy]-1-ethanol 313658-13-8P, 2-(2,5-Dimethoxyphenoxy)-1-ethanol 313658-20-7P, 3-Chloro-4-(1-piperazinyl)-1,2,5-thiadiazole 313658-22-9P, tert-Butyl 4-[3-[2-(2,3-Dihydro-1,4-benzodioxin-6-yloxy)ethoxy]-2-pyrazinyl]-1-piperazinecarboxylate 313658-32-1P, tert-Butyl (3R)-3-methyl-4-[3-[2-(3-pyridinyloxy)ethoxy]-2-pyrazinyl]-1-piperazinecarboxylate 313658-37-6P, tert-Butyl 4-[3-[(2-hydroxyethyl)sulfanyl]-2-pyrazinyl]-1-piperazinecarboxylate 313658-38-7P, tert-Butyl 4-[3-[(2-phenoxyethyl)sulfanyl]-2-pyrazinyl]-1-piperazinecarboxylate 313658-40-1P, tert-Butyl 4-[4-(2-hydroxyethoxy)-1,2,5-thiadiazol-3-yl]-1-piperazinecarboxylate 313658-41-2P, tert-Butyl 4-[4-[2-[(2-oxo-2H-chromen-7-yl)oxy]ethoxy]-1,2,5-thiadiazol-3-yl]-1-piperazinecarboxylate 313658-42-3P, tert-Butyl 4-[4-[2-(7-isoquinolinyloxy)ethoxy]-1,2,5-thiadiazol-3-yl]-1-piperazinecarboxylate 313658-46-7P, tert-Butyl 4-[3-[2-(3-hydroxyphenoxy)ethoxy]-2-pyrazinyl]-1-piperazinecarboxylate 313658-62-7P, tert-Butyl 4-[3-[2-[3-(2-methoxyethoxy)phenoxy]ethoxy]-2-pyrazinyl]-1-piperazinecarboxylate
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of heterocyclylpyrazinyl aryloxyalkyl ether 5-HT2C receptor agonists from aryloxyalkanols, halopyrazines, and heterocycles)

RE.CNT 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Anon; GB 1440722 1976 CAPLUS
(2) Anon; GB 1457005 1976 CAPLUS
(3) Anon; GB 1465946 1977 CAPLUS
(4) Anon; EP 0572863 A1 1993 CAPLUS
(5) Anon; EP 0655440 A2 1995 CAPLUS
(6) Anon; EP 0657426 A2 1995 CAPLUS
(7) Anon; WO 9501976 1995 CAPLUS
(8) Anon; EP 0711757 A1 1996 CAPLUS
(9) Anon; WO 9602525 A1 1996 CAPLUS
(10) Anon; WO 9611930 1996 CAPLUS
(11) Anon; DE 2433397 1997 CAPLUS
(12) Anon; CH 583715 1997 CAPLUS
(13) Anon; WO 9714689 1997 CAPLUS
(14) Anon; EP 0863136 A1 1998 CAPLUS
(15) Anon; WO 9842692 1998 CAPLUS
(16) Anon; WO 9903833 1999 CAPLUS
(17) Anon; WO 9958490 1999 CAPLUS
(18) Anon; WO 0012475 2000 CAPLUS
(19) Anon; WO 0012482 2000 CAPLUS
(20) Anon; WO 0012502 2000 CAPLUS
(21) Anon; WO 0012510 2000 CAPLUS
(22) Dourish, C; Obesity Research 1995, V3(4), P449
(23) Hori, M; Chem Pharm Bull 1993, V41(10), P1832 CAPLUS
(24) Jenck, F; Exp Opin Invest Drugs 1998, V7(10), P1587 CAPLUS
(25) Kennett, G; IDrugs 1998, V1(4), P456 CAPLUS
(26) Leysen, D; IDrugs 1999, V2(2), P109 CAPLUS
(27) Lumma, W; J of Med Chem 1978, V21(6), P536 CAPLUS
(28) Lumma, W; J of Med Chem 1981, V24, P93 CAPLUS
(29) Moser; US 3253989 A 1966 CAPLUS
(30) Rano, T; Tetrahedron Letters 1995, V36(22), P3789 CAPLUS
(31) Sargent, P; Psychopharmacology 1997, V133, P309 CAPLUS
(32) Tecott, L; Nature 1995, V374, P542 CAPLUS

L28 ANSWER 15 OF 21 CAPLUS

ACCESSION NUMBER: 2002:777933 CAPLUS
DOCUMENT NUMBER: 137:294969
TITLE: 4-Aryl-substituted 2-pyrimidinamines and 2-pyridinamines, useful as inhibitors of c-Jun N-terminal kinases (JNK) and other protein kinases
INVENTOR(S): Bethiel, Randy; Cochran, John; Moon, Young-Choon; Nanthakumar, Susanthini
PATENT ASSIGNEE(S): Vertex Pharmaceuticals Incorporated, USA
SOURCE: PCT Int. Appl., 115 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2002079197	A1	20021010	WO 2002-US9554		20020328
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
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US 2003087922	A1	20030508	US 2002-109070		20020328
EP 1373257	A1	20040102	EP 2002-725391		20020328
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PRIORITY APPLN. INFO.:			US 2001-279961P	P	20010329
			WO 2002-US9554	W	20020328

OTHER SOURCE(S): MARPAT 137:294969
AN 2002:777933 CAPLUS
DN 137:294969
ED Entered STN: 11 Oct 2002
TI 4-Aryl-substituted 2-pyrimidinamines and 2-pyridinamines, useful as inhibitors of c-Jun N-terminal kinases (JNK) and other protein kinases
IN Bethiel, Randy; Cochran, John; Moon, Young-Choon; Nanthakumar, Susanthini
PA Vertex Pharmaceuticals Incorporated, USA
SO PCT Int. Appl., 115 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07D405-04
ICS A61K031-506; C07D239-42; C07D213-74; A61K031-4418; A61P025-00; A61P037-00; A61P009-00; A61P029-00; C07D417-04; C07D403-04
CC 28-16 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 7
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2441733		AA	20021010	CA 2002-2441733	20020328
US 2003087922		A1	20030508	US 2002-109070	20020328
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PRAI US 2001-279961P		P	20010329		
WO 2002-US9554		W	20020328		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2002079197	ICM	C07D405-04
	ICS	A61K031-506; C07D239-42; C07D213-74; A61K031-4418; A61P025-00; A61P037-00; A61P009-00; A61P029-00; C07D417-04; C07D403-04
JP 2004529140	FTERM	4C055/AA01; 4C055/BA02; 4C055/BA52; 4C055/BB04; 4C055/BB07; 4C055/CA01; 4C055/DA08; 4C055/DA16; 4C055/DB01; 4C055/DB02; 4C055/FA01; 4C055/FA31; 4C055/FA37; 4C063/AA01; 4C063/BB01; 4C063/CC81; 4C063/CC82; 4C063/DD29; 4C063/EE01; 4C084/AA19; 4C084/NA14; 4C084/ZA022; 4C084/ZA162; 4C084/ZA182; 4C084/ZA342; 4C084/ZA362; 4C084/ZA402; 4C084/ZA542; 4C084/ZA592; 4C084/ZA892; 4C084/ZA922; 4C084/ZA942; 4C084/ZA962; 4C084/ZA972; 4C084/ZB052; 4C084/ZB072; 4C084/ZB082; 4C084/ZB112; 4C084/ZB152; 4C084/ZB212; 4C084/ZB262; 4C084/ZC202; 4C084/ZC212; 4C086/AA01; 4C086/AA02; 4C086/AA03; 4C086/AA04; 4C086/BC17; 4C086/BC42; 4C086/BC73; 4C086/GA02; 4C086/GA07; 4C086/MA01; 4C086/MA04; 4C086/NA14; 4C086/ZA02; 4C086/ZA16; 4C086/ZA18; 4C086/ZA34; 4C086/ZA36; 4C086/ZA40; 4C086/ZA54; 4C086/ZA59; 4C086/ZA89; 4C086/ZA92; 4C086/ZA94; 4C086/ZA96; 4C086/ZA97; 4C086/ZB05; 4C086/ZB07; 4C086/ZB08; 4C086/ZB11; 4C086/ZB15; 4C086/ZB21; 4C086/ZB26; 4C086/ZC20; 4C086/ZC21

OS MARPAT 137:294969

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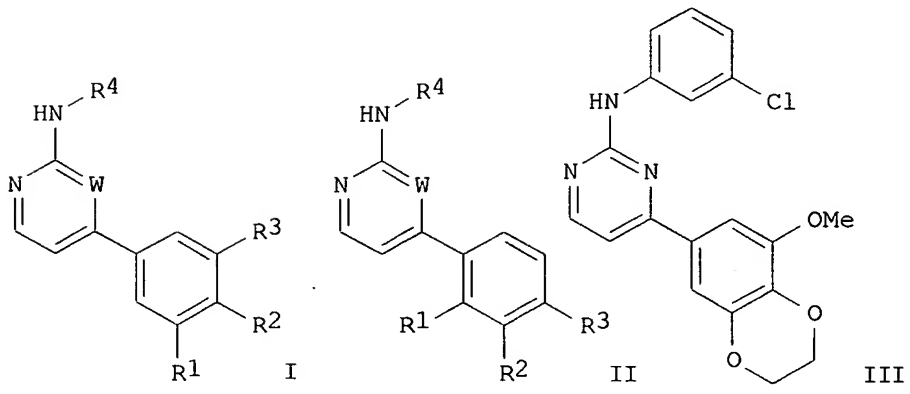

AB The invention provides compds. of formula I and II, and their

(1) Chiron Corp; WO 0220495 A 2002 CAPLUS
(2) Ciba Geigy Ag; WO 9509847 A 1995 CAPLUS
(3) Moffat, D; WO 9719065 A 1997 CAPLUS
(4) Moffat, D; WO 0129009 A 2001 CAPLUS
(5) Signal Pharm Inc; WO 0246170 A 2002 CAPLUS
(6) Signal Pharm Inc; WO 0246171 A 2002 CAPLUS

L28 ANSWER 16 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:391691 CAPLUS
DOCUMENT NUMBER: 136:386138
TITLE: Preparation of **piperazinylpyrazines** and analogs as serotonin 5HT-2 receptor modulators for treatment of CNS disorders
INVENTOR(S): Nilsson, Bjoern
PATENT ASSIGNEE(S): Biovitrum AB, Swed.
SOURCE: PCT Int. Appl., 97 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002040456	A1	20020523	WO 2001-SE2569	20011120
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AU 2002024266	A5	20020527	AU 2002-24266	20011120
US 2002147200	A1	20021010	US 2001-989358	20011120
US 6593330	B2	20030715		
EP 1335907	A1	20030820	EP 2001-996532	20011120
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BR 2001015400	A	20030930	BR 2001-15400	20011120
JP 2004532806	T2	20041028	JP 2002-542784	20011120
NO 2003002252	A	20030718	NO 2003-2252	20030519
US 2004014767	A1	20040122	US 2003-618868	20030714

PRIORITY APPLN. INFO.:	SE 2000-4245	A	20001120
	US 2000-253509P	P	20001128
	US 2001-989358	A3	20011120
	WO 2001-SE2569	W	20011120

OTHER SOURCE(S): MARPAT 136:386138
AN 2002:391691 CAPLUS
DN 136:386138
ED Entered STN: 24 May 2002
TI Preparation of **piperazinylpyrazines** and analogs as serotonin 5HT-2 receptor modulators for treatment of CNS disorders
IN Nilsson, Bjoern
PA Biovitrum AB, Swed.
SO PCT Int. Appl., 97 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07D241-18
ICS C07D241-20; C07D405-12; C07D213-82; C07D213-60; C07D213-64; C07D213-74; A61K031-497; A61K031-445; A61K031-4427; A61P025-00;

A61P025-18; A61P013-00; A61P025-04
CC 28-17 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1
FAN.CNT 1

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	NO 2003002252	A	20030718	NO 2003-2252	20030519
	US 2004014767	A1	20040122	US 2003-618868	20030714
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	US 2000-253509P	P	20001128		
	US 2001-989358	A3	20011120		
	WO 2001-SE2569	W	20011120		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2002040456	ICM	C07D241-18
	ICS	C07D241-20; C07D405-12; C07D213-82; C07D213-60; C07D213-64; C07D213-74; A61K031-497; A61K031-445; A61K031-4427; A61P025-00; A61P025-18; A61P013-00; A61P025-04
US 2002147200	ECLA	A61K031/4427; A61K031/445; A61K031/497; C07D213/64A; C07D239/46C3; C07D241/18; C07D241/20; C07D001/12+241B+217; C07D401/12+241B+215; C07D401/12+241B+209C; C07D401/12+241B+213; C07D405/04+307B241B; C07D405/12+307+241B; C07D405/12+307B+241B; C07D405/12+319+241B; C07D405/12+311C+241B; C07D409/04+333B+241B; C07D409/12+333+241B; C07D409/12+333B+241B; C07D409/14+33B+241B+207; C07D413/12+263B+241B
JP 2004532806	FTERM	4C063/AA01; 4C063/AA03; 4C063/BB01; 4C063/BB08; 4C063/CC34; 4C063/CC52; 4C063/CC75; 4C063/CC81; 4C063/CC92; 4C063/DD04; 4C063/DD06; 4C063/DD34; 4C063/EE01; 4C086/AA02; 4C086/AA03; 4C086/BC42; 4C086/BC48; 4C086/BC50; 4C086/BC69; 4C086/GA02; 4C086/GA04; 4C086/GA07; 4C086/GA08; 4C086/GA09; 4C086/GA12; 4C086/MA02; 4C086/MA05; 4C086/NA14; 4C086/ZA01; 4C086/ZA08; 4C086/ZA15; 4C086/ZA66; 4C086/ZA70; 4C086/ZA81; 4C086/ZC02; 4C086/ZC39
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C07D409/12+333+241B; C07D409/12+333B+241B;
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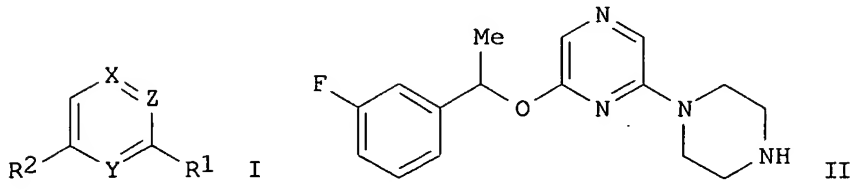
OS MARPAT 136:386138

GI



I II

AB Title compds. I [wherein X and Y = N and Z = CH, forming a pyrazine derivative; or X and Z = CH and Y = N, forming a pyridine derivative; or X = C(CF3), Z = CH, and Y = N, forming a 4-trifluoromethylpyridine derivative; or Y and Z = N and X = CH, forming a pyrimidine derivative; R1 and R2 = independently (hetero)arylalkyl, (hetero)arylalkoxy, indanyloxy, (hetero)aryloxy, (hetero)arylthio, (cyclo)alkylthio, (cyclo)alkoxy, fluoroalkoxy, alkynyloxy, alkenyloxy, cycloalkylalkoxy, halo, (hetero)arylalkylthio, (hetero)arylamino, (hetero)aryl, or (un)substituted **piperazinyl** or piperidinyloxy with provisos; and pharmaceutically acceptable salts, hydrates, isomers, tautomers, N-oxides, and prodrugs thereof] were prepared as 5HT2C agonists and antagonists. For example, 2,6-dichloropyrazine was treated with 1-(3-fluorophenyl)ethanol and NaH in dioxane to give 2-chloro-6-[1-(3-fluorophenyl)ethoxy]pyrazine. Addition of **piperazine** and K2CO3 in AcCN and heating under reflux overnight afforded II. The latter bound to membranes, prepared from transfected HEK293 cell line stably expressing the human 5-HT2C receptor protein, with Ki of 8 nM in competition expts. In addition, I exhibited agonist efficacy at the 5-HT2C receptor by mobilizing intracellular Ca in transfected cells with maximum responses in the range of 20-100% relative to the maximum response of serotonin at concns. of 1 μM. I are useful for the treatment of serotonin-related CNS disorders, such as eating disorders, obesity, memory disorder, anxiety, sexual dysfunction, epilepsy, urinary disorders, pain, substance abuse, and **schizophrenia** (no data).

ST **piperazinylpyrazine** prepn serotonin 5HT2 receptor modulator; pyrazine **piperazinyl** prepn CNS agents

IT Drugs of abuse
(abuse of, treatment; preparation of **piperazinylpyrazines** and analogs as serotonin 5HT2C receptor modulators for treatment of CNS disorders)

IT Appetite
Sexual behavior
(disorder, treatment; preparation of **piperazinylpyrazines** and analogs as serotonin 5HT2C receptor modulators for treatment of CNS disorders)

IT Bladder, disease
(incontinence, treatment; preparation of **piperazinylpyrazines** and analogs as serotonin 5HT2C receptor modulators for treatment of CNS disorders)

IT Mental disorder
(mood-affecting, treatment; preparation of **piperazinylpyrazines** and analogs as serotonin 5HT2C receptor modulators for treatment of CNS disorders)

IT 5-HT agonists
5-HT antagonists
Analgesics
Anticonvulsants
Antiobesity agents
Anxiolytics

1,3-thiazol-2-yl)amino]-2-oxoethyl]-1,4,5,6-tetrahydroazepino[4,5-b]indole-3(2H)-carboxylate 405311-57-1, tert-Butyl 10-bromo-6-[2-[(4-methyl-**1,3-thiazol**-2-yl)amino]-2-oxoethyl]-1,4,5,6-tetrahydroazepino[4,5-b]indole-3(2H)-carboxylate 405312-01-8, 10-(2,4-Dichlorophenyl)-1,2,3,4,5,6-hexahydroazepino[4,5-b]indole 405312-58-5, 10-[3-(2-Chlorophenoxy)propyl]-1,2,3,4,5,6-hexahydroazepino[4,5-b]indole 405312-60-9, 10-(2-Phenylethyl)-1,2,3,4,5,6-hexahydroazepino[4,5-b]indole 405312-62-1, 10-[3-(2-Naphthyloxy)propyl]-1,2,3,4,5,6-hexahydroazepino[4,5-b]indole 405312-64-3, 10-(3-Phenoxypropyl)-1,2,3,4,5,6-hexahydroazepino[4,5-b]indole 405313-24-8, Di(tert-butyl) 10-bromo-1,2,4,5,5a,10b-hexahydroazepino[4,5-b]indole-3,6-dicarboxylate 405313-34-0, 9,10-Dichloro-6-(2-phenoxyethyl)-1,2,3,4,5,5a,6,10b-octahydroazepino[4,5-b]indole 405313-38-4, 7,10-Dichloro-6-(2-phenoxyethyl)-1,2,3,4,5,6-hexahydroazepino[4,5-b]indole 405313-40-8, 7,8-Dichloro-6-(2-phenoxyethyl)-1,2,3,4,5,6-hexahydroazepino[4,5-b]indole 405313-42-0, 8,10-Dichloro-6-(2-phenoxyethyl)-1,2,3,4,5,6-hexahydroazepino[4,5-b]indole
RL: RCT (Reactant); RACT (Reactant or reagent)
(reactant; preparation of azepino[4,5-b]indolines as 5-HT receptor ligands for treatment of central nervous system disorders)

L28 ANSWER 18 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:730745 CAPLUS
DOCUMENT NUMBER: 135:288799
TITLE: Preparation of 2,3,4,5-tetrahydro-1H-[1,4]diazepino[1,7-a]indoles as 5-HT receptor antagonists for treatment of CNS disorders
INVENTOR(S): Ennis, Michael Dalton; Hoffman, Robert Louis; Ghazal, Nabil B.; Olson, Rebecca M.
PATENT ASSIGNEE(S): Pharmacia & Upjohn Co., USA
SOURCE: PCT Int. Appl., 331 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001072752	A2	20011004	WO 2001-US4950	20010308
WO 2001072752	A3	20030417		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
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AU 2001043163	A5	20011008	AU 2001-43163	20010308
US 2002002161	A1	20020103	US 2001-803242	20010308
US 6734301	B2	20040511		
EP 1328525	A2	20030723	EP 2001-916099	20010308
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2003529569	T2	20031007	JP 2001-570662	20010308
ZA 2002007341	A	20040121	ZA 2002-7341	20020912
US 2004209870	A1	20041021	US 2004-761070	20040120
PRIORITY APPLN. INFO.:			US 2000-189103P P	20000314

US 2001-803242 A3 20010308
WO 2001-US4950 W 20010308

OTHER SOURCE(S): MARPAT 135:288799
AN 2001:730745 CAPLUS
DN 135:288799
ED Entered STN: 07 Oct 2001
TI Preparation of 2,3,4,5-tetrahydro-1H-[1,4]diazepino[1,7-a]indoles as 5-HT receptor antagonists for treatment of CNS disorders
IN Ennis, Michael Dalton; Hoffman, Robert Louis; Ghazal, Nabil B.; Olson, Rebecca M.
PA Pharmacia & Upjohn Co., USA
SO PCT Int. Appl., 331 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07D487-04
ICS A61K031-5517; A61P025-00; C07D209-18; C07D487-04; C07D243-00; C07D209-00
CC 28-21 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001072752	A2	20011004	WO 2001-US4950	20010308
	WO 2001072752	A3	20030417		
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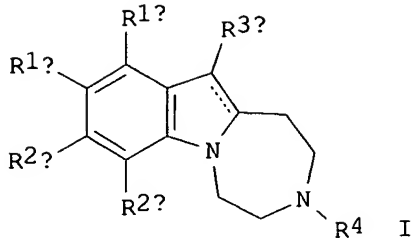
	US 2002002161	A1	20020103	US 2001-803242	20010308
	US 6734301	B2	20040511		
	EP 1328525	A2	20030723	EP 2001-916099	20010308
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	JP 2003529569	T2	20031007	JP 2001-570662	20010308
	ZA 2002007341	A	20040121	ZA 2002-7341	20020912
	US 2004209870	A1	20041021	US 2004-761070	20040120
PRAI	US 2000-189103P	P	20000314		
	US 2001-803242	A3	20010308		
	WO 2001-US4950	W	20010308		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2001072752	ICM	C07D487-04
	ICS	A61K031-5517; A61P025-00; C07D209-18; C07D487-04; C07D243-00; C07D209-00
US 2002002161	ECLA	C07D209/18; C07D487/04+243C+209C
US 2004209870	ECLA	C07D209/18; C07D487/04+243C+209C

OS MARPAT 135:288799
GI



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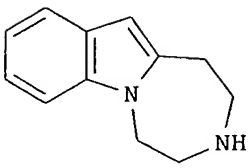

II

AB Title compds. I [wherein R1a, R1b, R2a, and R2b = independently (a) H, halo, CN, CF3, OCF3, OR5, CONR5R6, COR5, CO2R5, Y(CH2)mXR5, YCO(CH2)mXR5; m = 0-3; Y = CH2, S, O, or NR6; X = CH2, S, O, NR6; (b) (CH2)pAr; p = 0-3; Ar = (un)substituted (hetero)aryl or (c) (un)substituted (cyclo)alkyl, (cyclo)alkenyl, or (cyclo)alkynyl; R3 = (a) H, halo, CN, CF3, OCF3, alkyl, Ar, OR5, SR5, CHO, CONR5R6, COR5, CO2R5, Yo(CH2)nXR5, COCONXR5, Yo(CH2)nN(R6)CONR5R6; o = 0 or 1; n = 0-3; X = CH, S, O, or NR6; Y = CH, S, O or NR6; Ar = (un)substituted (hetero)aryl; (b) (un)substituted (cyclo)alkyl, (cyclo)alkenyl, or (cyclo)alkynyl; R4, R5, and R6 = independently (a) H or (un)substituted (cyclo)alkyl, (cyclo)alkenyl, or (cyclo)alkynyl; (b) (CH2)pAr; p = 0-3; Ar = (un)substituted (hetero)aryl; or stereoisomers or pharmaceutically acceptable salts thereof] were prepared For example, 2,3,4,5-tetrahydro-1H-[1,4]diazepino[1,7-a]indole•HCl (II•HCl) was prepared in a multi-step synthesis starting from Et H malonate and 2-nitrophenylacetic acid and involving the cyclization of the Et [1-(2-bromoethyl)-2,3-dihydro-1H-indol-2-yl]acetate intermediate to the tetrahydro-1H-[1,4]diazepino[1,7]indol-2(3H)-one. I are useful as 5-HT receptor antagonists for the treatment of a variety of central nervous system disorders (no data).

ST diazepinoindole prepn 5HT receptor antagonist; central nervous system disorder treatment diazepinoindole prepn

IT Mental disorder
(affective, seasonal, treatment; preparation of 1H-[1,4]diazepino[1,7-a]indoles as 5-HT receptor inhibitors for treatment of CNS disorders)

IT Mental disorder
(attention deficit disorder, treatment; preparation of 1H-[1,4]diazepino[1,7-a]indoles as 5-HT receptor inhibitors for treatment of CNS disorders)

IT Mental disorder
(attention deficit hyperactivity disorder, treatment; preparation of 1H-[1,4]diazepino[1,7-a]indoles as 5-HT receptor inhibitors for treatment of CNS disorders)

IT Mental disorder
(autism, treatment; preparation of 1H-[1,4]diazepino[1,7-a]indoles as 5-HT receptor inhibitors for treatment of CNS disorders)

IT Appetite
(bulimia, treatment; preparation of 1H-[1,4]diazepino[1,7-a]indoles as 5-HT receptor inhibitors for treatment of CNS disorders)

IT Nervous system
(central, disease, treatment; preparation of 1H-[1,4]diazepino[1,7-a]indoles as 5-HT receptor inhibitors for treatment of CNS disorders)

IT Fatigue, biological
(chronic fatigue syndrome, treatment; preparation of 1H-[1,4]diazepino[1,7-a]indoles as 5-HT receptor inhibitors for treatment of CNS disorders)

IT Nervous system
(degeneration, treatment; preparation of 1H-[1,4]diazepino[1,7-a]indoles as 5-HT receptor inhibitors for treatment of CNS disorders)

IT Sexual behavior
(disorder, treatment; preparation of 1H-[1,4]diazepino[1,7-a]indoles as 5-HT receptor inhibitors for treatment of CNS disorders)

3528-58-3 3740-52-1, 2-Nitrophenylacetic acid 4005-51-0, 1,3,4-Thiadiazol-2-amine 4837-88-1, 2-Methyl-3-nitroanisole 5049-61-6, 2-Pyrazinylamine 5150-42-5, 2,3-Dimethoxyphenol 5345-54-0, 3-Chloro-p-anisidine 5464-79-9 6285-57-0, 6-Nitro-1,3-benzothiazol-2-ylamine 6636-78-8, 2-Chloro-3-pyridinol 6968-35-0, 7-Hydroxy-1-indanone 7305-71-7 7368-78-7, 4-Bromoguaiacol 10288-36-5, 2,3-Dihydro-1,4-benzodioxin-5-ol 13519-75-0 14678-02-5 15599-52-7, 5,7-Dibromo-2-methyl-8-quinolinol 16582-59-5 19952-47-7 24072-75-1 24340-76-9 28315-93-7, 5-Hydroxy-3,4-dihydro-1(2H)naphthalenone 29558-77-8 29927-08-0 30273-42-8 33332-28-4 37873-29-3, 5,7-Dimethyl-8-quinolinol 40731-98-4, 4-Hydroxy-1-indanone 41175-50-2 54396-44-0, 2-Methyl-3-(trifluoromethyl)phenylamine 57946-56-2 58327-60-9, 7-Propyl-8-quinolinol 61424-26-8 64036-71-1 73943-41-6, 2-Fluoro-6-methoxyphenol 76064-17-0 77326-36-4 90843-62-2, 6-Hydroxy-5-methoxy-1-indanone 91133-00-5, 2-Acetyl-1,2,3,4-tetrahydro-5-isoquinolinol 94250-82-5 119256-40-5, 4,6-Difluoro-1,3-benzothiazol-2-ylamine 135050-44-1 135187-61-0 171979-69-4, 5,5-Dimethyl-5,6,7,8-tetrahydro-1-naphthalenol 207291-85-8 364344-72-9 364344-80-9 364345-16-4 364346-30-5 364346-82-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(reactant; preparation of 1H-[1,4]diazepino[1,7-a]indoles as 5-HT receptor inhibitors for treatment of CNS disorders)

L28 ANSWER 19 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:693264 CAPLUS
DOCUMENT NUMBER: 135:257269
TITLE: Preparation of N-heterocyclyl amide compounds as 5-HT antagonists
INVENTOR(S): Yamada, Akira; Tomishima, Masaki; Hayashida, Hisashi; Imanishi, Masashi; Spears, Glen W.; Ito, Kiyotaka; Takahashi, Fumie; Miyake, Hiroshi
PATENT ASSIGNEE(S): Fujisawa Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 239 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2001068585	A1	20010920	WO 2001-JP1993		20010313
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
AU 2001041128	A5	20010924	AU 2001-41128		20010313
EP 1264820	A1	20021211	EP 2001-912338		20010313
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
US 2004087798	A1	20040506	US 2002-221554		20021227
PRIORITY APPLN. INFO.:			JP 2000-70127	A	20000314
			JP 2000-305947	A	20001005
			WO 2001-JP1993	W	20010313

OTHER SOURCE(S): CASREACT 135:257269; MARPAT 135:257269
AN 2001:693264 CAPLUS
DN 135:257269
ED Entered STN: 21 Sep 2001
TI Preparation of N-heterocyclyl amide compounds as 5-HT antagonists

IN Yamada, Akira; Tomishima, Masaki; Hayashida, Hisashi; Imanishi, Masashi; Spears, Glen W.; Ito, Kiyotaka; Takahashi, Fumie; Miyake, Hiroshi
PA Fujisawa Pharmaceutical Co., Ltd., Japan
SO PCT Int. Appl., 239 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
IC ICM C07C233-75
ICS C07C233-80; C07C233-81; C07C257-14; C07C257-18; C07C257-20; C07D233-64; C07D249-08; C07D239-26; C07D213-75; C07D231-12; C07D217-22; C07D333-20; C07D277-28; C07D263-32; C07D233-36; C07D215-12; C07D209-08; C07D405-12; C07D403-12
CC 28-19 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001068585	A1	20010920	WO 2001-JP1993	20010313
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 2001041128	A5	20010924	AU 2001-41128	20010313
EP 1264820	A1	20021211	EP 2001-912338	20010313
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
US 2004087798	A1	20040506	US 2002-221554	20021227
PRAI JP 2000-70127	A	20000314		
JP 2000-305947	A	20001005		
WO 2001-JP1993	W	20010313		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2001068585	ICM	C07C233-75
	ICS	C07C233-80; C07C233-81; C07C257-14; C07C257-18; C07C257-20; C07D233-64; C07D249-08; C07D239-26; C07D213-75; C07D231-12; C07D217-22; C07D333-20; C07D277-28; C07D263-32; C07D233-36; C07D215-12; C07D209-08; C07D405-12; C07D403-12
EP 1264820	ECLA	C07C233/75

OS CASREACT 135:257269; MARPAT 135:257269
AB Amides compds. represented by the general formula R1-A-X-NHCO-Y-R2 [wherein R1 is an optionally substituted heterocyclic group or optionally substituted phenyl; R2 is optionally substituted fused Ph, optionally substituted Ph, or optionally substituted thienyl; A is a group represented by the formula -(CH2)t-(O)m- or -(CR3R4)pNR5(CO)n- (wherein R3 and R4 each is hydrogen or R3 and R4 in combination form imino; R5 is hydrogen or lower alkyl; t is 0, 1, or 2; and p, m, and n each is 0 or 1); X is optionally substituted phenylene or an optionally substituted, divalent, nitrogenous heterocyclic group; and Y is a bond, lower alkylene, or lower alkenylene] and salts thereof are prepared Theses amides include phenylacetamide, cinnamides, 1H-indole-7-carboxamides, 3-(2-pyridyl)-2-propenamides, 5-phenyl-2-thiophenecarboxamides, 9H-carbazolecarboxamides, 3-phenyl-2-propenamides, 9H-fluorene-1-carboxamides, 2,3-dihydrobenz[b]oxepine-4-carboxamides, 1H-benzo[b]thiepin-4-carboxamides, and 3-(1H-indol-3-yl)-2-propenamides. They are antagonists of 5-hydroxytryptamine (5-HT), in particular 5-HT2c, and are useful for the treatment of 5-HT-mediated diseases such as (1) central nervous system disorders in including anxiety, depression,

obsessive-compulsive neurosis, migraine headache, anorexia, Alzheimer's disease, sleep disorder, over-eating, and panic, (2) withdrawal symptom caused by cocaine, ethanol, nicotine, and benzodiazepine, (3) **schizophrenia**, (4) spinal cord injury, and /or (5) head injury such as hydrocephalus. Thus, SOCl2 was added to a solution of (E)-4-phenyl-3-butenoic acid in benzene, heated under reflux for 1 h, and cooled, followed by adding 3-(imidazol-1-yl)aniline and Et3N, and the resulting mixture was stirred at room temperature for 1 h to give (3E)-N-[3-(imidazol-1-yl)phenyl]-4-phenyl-3-butenamide (I). I in vitro inhibited by 82% the binding of [3H]mesulergine to 5-HT2c receptor which was prepared from rat frontal lobe cortex.

ST amide prepn hydroxytryptamine 5HT antagonist; phenylacetamide prepn hydroxytryptamine 5HT2c antagonist; cinnamide prepn hydroxytryptamine 5HT2c antagonist; indolecarboxamide prepn treatment head injury; pyridylpropenamide prepn hydroxytryptamine 5HT2c antagonist; phenylthiophenecarboxamide prepn hydroxytryptamine 5HT2c antagonist; carbazolecarboxamide prepn hydroxytryptamine 5HT2c antagonist; phenylpropenamide prepn hydroxytryptamine 5HT2c antagonist; fluorenecarboxamide prepn central nervous system agent; dihydrobenzoxepincarboxamide prepn treatment drug withdrawal symptom; benzothiepincarboxamide prepn treatment **schizophrenia**; indolylpropenamide prepn treatment spinal code injury 456312

IT 5-HT receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study); PROC (Process)
(5-HT2C, antagonists; preparation of N-heterocyclyl amide compds. as 5-HT antagonists for treatment of 5-HT-mediated diseases such as central nervous system disorders, drug withdrawal symptom, **schizophrenia**, spinal cord injury, and head injury)

IT Sleep
(disorder; preparation of N-heterocyclyl amide compds. as 5-HT antagonists for treatment of 5-HT-mediated diseases such as central nervous system disorders, drug withdrawal symptom, **schizophrenia**, spinal cord injury, and head injury)

IT Appetite
(hyperphagia; preparation of N-heterocyclyl amide compds. as 5-HT antagonists for treatment of 5-HT-mediated diseases such as central nervous system disorders, drug withdrawal symptom, **schizophrenia**, spinal cord injury, and head injury)

IT Head
Spinal cord
(injury; preparation of N-heterocyclyl amide compds. as 5-HT antagonists for treatment of 5-HT-mediated diseases such as central nervous system disorders, drug withdrawal symptom, **schizophrenia**, spinal cord injury, and head injury)

IT Headache
(migraine; preparation of N-heterocyclyl amide compds. as 5-HT antagonists for treatment of 5-HT-mediated diseases such as central nervous system disorders, drug withdrawal symptom, **schizophrenia**, spinal cord injury, and head injury)

IT Mental disorder
(neurosis, obsessive-compulsive; preparation of N-heterocyclyl amide compds. as 5-HT antagonists for treatment of 5-HT-mediated diseases such as central nervous system disorders, drug withdrawal symptom, **schizophrenia**, spinal cord injury, and head injury)

IT Anxiety
(panic; preparation of N-heterocyclyl amide compds. as 5-HT antagonists for treatment of 5-HT-mediated diseases such as central nervous system disorders, drug withdrawal symptom, **schizophrenia**, spinal cord injury, and head injury)

IT 5-HT antagonists
Alzheimer's disease
Anorexia

Antidepressants
Anxiolytics
Drug withdrawal
Nervous system agents
Schizophrenia
(preparation of N-heterocyclyl amide compds. as 5-HT antagonists for treatment of 5-HT-mediated diseases such as central nervous system disorders, drug withdrawal symptom, **schizophrenia**, spinal cord injury, and head injury)

IT Amides, preparation
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of N-heterocyclyl amide compds. as 5-HT antagonists for treatment of 5-HT-mediated diseases such as central nervous system disorders, drug withdrawal symptom, **schizophrenia**, spinal cord injury, and head injury)

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RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of N-heterocyclyl amide compds. as 5-HT antagonists for

treatment of 5-HT-mediated diseases such as central nervous system disorders, drug withdrawal symptom, **schizophrenia**, spinal code injury, and head injury)

IT 75-65-0, tert-Butyl alcohol, reactions 110-91-8, **Morpholine**, reactions 367-31-7, 4-Fluoro-1,2-benzenediamine 462-08-8, 3-Aminopyridine 504-24-5, 4-Aminopyridine 591-54-8, 4-Aminopyrimidine 624-83-9, Methyl isocyanate 814-75-5, 2-Bromo-3-butanone 939-58-2, trans-2-Chlorocinnamic acid 940-62-5, (E)-3-(4-Chlorophenyl)acrylic acid 1068-57-1, Acetylhydrazine 1121-60-4, 2-Formylpyridine 1722-12-9, 2-Chloropyrimidine 1914-58-5, (E)-4-Phenyl-3-butenoic acid 2062-25-1, 3-[2-(Trifluoromethyl)phenyl]acrylic acid 2706-56-1, 2-(2-Pyridyl)ethylamine 2759-28-6, 1-Benzylpiperazine 3529-82-6, 3-Nitrophenyl isothiocyanate 3731-52-0, 3-Pyridinemethanamine 4110-35-4, 3,5-Dinitrobenzonitrile 4595-59-9, 5-Bromopyrimidine 5327-44-6, 3,5-Dinitroanisole 5720-06-9, 2-Methoxyphenylboronic acid 5873-89-2 6276-03-5, 9H-Fluorene-1-carboxylic acid 6952-67-6, 2-(3-Nitrophenyl)-1,3-dioxolane 13026-12-5, 3-(Naphthalen-1-yl)acrylic acid 13026-23-8, 3-(1,1'-Biphenyl-4-yl)acrylic acid 13331-27-6, 3-Nitrophenylboronic acid 14473-90-6, (E)-3-(3-Chlorophenyl)acrylic acid 16263-52-8, 3-Chloro-1,2-benzisoxazole 16642-92-5, (E)-3-(4-Trifluoromethylphenyl)acrylic acid 20010-99-5, 2-Aminomethylpyrazine 20595-44-2, (E)-3-(2,3-Dichlorophenyl)acrylic acid 20595-45-3, (E)-3-(2,4-Dichlorophenyl)acrylic acid 20826-04-4, 5-Bromonicotinic acid 21035-59-6 21630-48-8 . 22280-56-4, 2-Chloro-3-methyl-5-nitropyridine 26177-43-5, 3-Nitrobenzylamine hydrochloride 33786-89-9, 3,5-Diaminochlorobenzene 36052-25-2, 5-Aminonicotinic acid methyl ester 59002-79-8, 6-Fluoro-9H-carbazole-1-carboxylic acid 63413-91-2, 3-Phenylthioacrylic acid 69491-59-4, 3-(5-Pyrimidinyl)aniline 83823-06-7, 6-Chloro-2H-chromene-3-carboxylic acid 89260-48-0 89640-55-1, 3-Iodo-4-methoxypyridine 89878-14-8, Diethyl(3-pyridyl)borane 99368-67-9, 2-Chloro-5-nitro-3-(trifluoromethyl)pyridine 112677-67-5, 3-(Imidazol-1-yl)aniline 112898-33-6, (E)-3-(2,5-Difluorophenyl)acrylic acid 123947-73-9, 7-Methoxy-2,3-dihydrobenz[b]oxepin-4-carboxylic acid 123947-74-0, 8-Methoxy-2,3-dihydrobenz[b]oxepin-4-carboxylic acid 129768-95-2 135616-29-4, 8,9-Dihydro-7H-benzocycloheptene-6-carboxylic acid 138830-47-4, 4-Methyl-1-(3-nitrophenyl)-1H-imidazole 147700-58-1, (E)-3-(3,4-Difluorophenyl)acrylic acid 153936-26-6 174603-37-3, (E)-3-(2-Chloro-4-fluorophenyl)acrylic acid 176032-78-3 181633-42-1, 3-Amino-6-(2-methyl-3-pyridyloxy)pyridine 206353-51-7, 2,3-Dihydrobenz[b]oxepin-4-carboxylic acid 312619-48-0, (E)-3-[2,5-Bis(trifluoromethyl)phenyl]acrylic acid 326476-49-7 333792-46-4, 3-(1,2-Dimethylimidazol-5-yl)aniline 333792-92-0, 3-Methyl-2-(trifluoromethyl)-1H-indole-7-carboxylic acid 333793-36-5, 3-(4,5-Dimethylimidazol-1-yl)aniline 361549-63-5 361549-97-5 361550-35-8 361550-60-9 361551-42-0 361551-53-3 361551-64-6 361551-84-0 361551-95-3 361551-98-6 361552-00-3 361552-08-1 361552-10-5 361552-12-7 361552-15-0 361552-32-1

RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of N-heterocyclyl amide compds. as 5-HT antagonists for treatment of 5-HT-mediated diseases such as central nervous system disorders, drug withdrawal symptom, **schizophrenia**, spinal code injury, and head injury)

IT 6398-87-4P, 3-(1,3-Dioxolan-2-yl)aniline 10406-92-5P, 3-Cyano-5-nitroaniline 21626-42-6P 21630-51-3P 55341-64-5P, 9H-Fluorene-1-carbonyl chloride 167897-26-9P 361549-59-9P 361549-62-4P 361549-64-6P 361549-65-7P 361549-66-8P 361549-67-9P 361549-68-0P 361549-69-1P 361549-70-4P 361549-71-5P 361549-72-6P 361549-73-7P 361549-74-8P 361549-75-9P 361549-76-0P 361549-80-6P 361549-81-7P 361549-82-8P 361549-83-9P 361549-84-0P 361549-85-1P 361549-86-2P 361549-87-3P 361549-88-4P 361549-89-5P 361549-90-8P 361549-91-9P 361549-92-0P 361549-93-1P 361549-94-2P 361549-95-3P 361549-96-4P 361549-98-6P 361549-99-7P 361550-00-7P 361550-01-8P

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RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of N-heterocyclyl amide compds. as 5-HT antagonists for treatment of 5-HT-mediated diseases such as central nervous system disorders, drug withdrawal symptom, **schizophrenia**, spinal code injury, and head injury)

IT 62-55-5, Thioacetamide 74-88-4, Methyl iodide, reactions 99-09-2, 3-Nitroaniline 99-29-6, 2-Bromo-6-chloro-4-nitroaniline 99-61-6, 3-Nitrobenzaldehyde 99-81-0, 2-Bromo-1-(4-nitrophenyl)ethanone 103-82-2, Phenylacetic acid, reactions 288-13-1, Pyrazole 345-16-4, 5-Fluoro-2-hydroxybenzoic acid 350-46-9, 4-Fluoro-1-nitrobenzene 364-76-1, 4-Fluoro-3-nitroaniline 621-82-9, Cinnamic acid, reactions 1194-02-1, 4-Fluorobenzonitrile 1739-84-0, 1,2-Dimethylimidazole 3731-51-9, 2-(Aminomethyl)pyridine 3752-25-8, 2-Chlorocinnamic acid 3819-88-3, 1-Fluoro-3-iodo-5-nitrobenzene 4548-45-2, 2-Chloro-5-nitropyridine 13889-98-0, 1-Acetylpiperazine 14432-12-3, 4-Amino-2-chloropyridine 18197-26-7 18437-64-4, tert-Butyl 3-nitrophenylcarbamate 24424-99-5, Di-tert-butyl dicarbonate 68621-88-5, tert-Butyl 3-aminophenylcarbamate
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of N-heterocyclyl amide compds. as 5-HT antagonists for treatment of 5-HT-mediated diseases such as central nervous system disorders, drug withdrawal symptom, **schizophrenia**, spinal cord injury, and head injury)

IT 704-04-1P, 5-Fluoro-2-methoxybenzamide 1008-95-3P, 4-(1,3-Oxazol-5-yl)aniline 1014-23-9P, 5-(4-Nitrophenyl)-1,3-oxazole 3463-30-7P, 1-(4-Nitrophenyl)-1H-pyrazole 3704-42-5P, 4-(4-Nitrophenyl)-1,3-thiazole 13140-76-6P, N-(3-Nitrophenyl)phenylacetamide 17635-45-9P, 4-(1H-Pyrazol-1-yl)aniline 23068-80-6P, 5-Chloro-2-methoxybenzamide 33786-93-5P, 3,5-Diaminobenzonitrile 33924-48-0P, Methyl 5-chloro-2-methoxybenzoate 38980-93-7P, 4-(4-Nitrophenyl)-1H-imidazole 55000-38-9P, N-(3-Nitrophenyl)cinnamide 55877-79-7P, 5-Chloro-2-methoxybenzonitrile 60759-10-6P, 4-(**1,3-Thiazol**-4-yl)aniline 85856-32-2P, N-(3-Aminophenyl)phenylacetamide 89250-16-8P, 4-(1-Methyl-1H-imidazol-4-yl)aniline 103298-41-5P, 1-Methyl-4-(4-nitrophenyl)-1H-imidazole 151793-20-3P, Methyl 5-fluoro-2-methoxybenzoate 186650-90-8P, 4-(4-Acetyl-1-piperazinyl)benzonitrile 189628-38-4P, 5-Fluoro-2-methoxybenzonitrile 219817-43-3P, 3-Bromo-5-chloronitrobenzene 332370-72-6P, tert-Butyl 4-fluoro-3-nitrophenylcarbamate 349433-63-2P, N-(4-Cyanophenyl)-2-chlorocinnamide 361548-78-9P 361548-79-0P 361548-80-3P, 5-(3-Methoxy-5-nitrophenyl)-1,2-dimethyl-1H-imidazole 361548-81-4P 361548-82-5P 361548-83-6P
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RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT

(Reactant or reagent)
(preparation of N-heterocyclyl amide compds. as 5-HT antagonists for treatment of 5-HT-mediated diseases such as central nervous system disorders, drug withdrawal symptom, **schizophrenia**, spinal cord injury, and head injury)

RE.CNT 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Dr A Wander SA; GB 1007334 A1 1965 CAPLUS
(2) Fisons Corporation; EP 690851 A1 1994 CAPLUS
(3) Fisons Corporation; WO 94/21621 A1 1994 CAPLUS
(4) Fisons Corporation; JP 09-501918 A 1995
(5) Fisons Corporation; EP 713483 A1 1995 CAPLUS
(6) Fisons Corporation; WO 95/05363 A1 1995 CAPLUS
(7) Fujisawa Pharmaceutical Co, Ltd; JP 11-349572 A 1999 CAPLUS
(8) Fujisawa Pharmaceutical Co, Ltd; JP 11-130750 A 1999 CAPLUS
(9) Kalkman, H; Eur J Pharmacol 1998, V343(2/3), P201 CAPLUS
(10) Konica Corporation; JP 03-282536 A 1991 CAPLUS
(11) Konica Corporation; JP 04-76530 A 1992 CAPLUS
(12) Korbonits, D; Chem Ber 1984, V117(11), P3183 CAPLUS
(13) Manuel, N; Br J Pharmacol 1995, V116(6), P2647 CAPLUS
(14) Nippon Soda Co, Ltd; WO 00/06550 A1 2000 CAPLUS
(15) Nippon Soda Co, Ltd; EP 1101759 A1 2000 CAPLUS
(16) Smithkline Beecham PLC; JP 09-501171 A 1995
(17) Smithkline Beecham PLC; JP 09-504004 A 1995
(18) Smithkline Beecham PLC; JP 09-512804 A 1995
(19) Smithkline Beecham PLC; EP 712397 A1 1995 CAPLUS
(20) Smithkline Beecham PLC; EP 714389 A1 1995 CAPLUS
(21) Smithkline Beecham PLC; EP 758330 A1 1995 CAPLUS
(22) Smithkline Beecham PLC; WO 95/04729 A1 1995 CAPLUS
(23) Smithkline Beecham PLC; WO 95/06044 A1 1995 CAPLUS
(24) Smithkline Beecham PLC; WO 95/30675 A1 1995 CAPLUS
(25) Smithkline Beecham PLC; JP 10-513442 A 1996
(26) Smithkline Beecham PLC; JP 10-513443 A 1996
(27) Smithkline Beecham PLC; EP 807104 A2 1996 CAPLUS
(28) Smithkline Beecham PLC; EP 808312 A1 1996 CAPLUS
(29) Smithkline Beecham PLC; WO 96/23769 A2 1996 CAPLUS
(30) Smithkline Beecham PLC; WO 96/23783 A1 1996 CAPLUS
(31) Societe de Conseils de Recherches et d'Applications Scientifiques; EP 973763 A1 1998 CAPLUS
(32) Societe de Conseils de Recherches et d'Applications Scientifiques; WO 98/42696 A1 1998 CAPLUS

L28 ANSWER 20 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2001:283789 CAPLUS

DOCUMENT NUMBER: 134:311210

TITLE: 5-Membered heterocycle derivatives useful as monoamine oxidase inhibitors, lipid peroxidation inhibitors, and sodium channel modulators, and the production thereof, and use thereof as medicaments

INVENTOR(S): Chabrier de Lassauniere, Pierre-Etienne; Harnett, Jeremiah; Bigg, Dennis; Pommier, Jacques; Lannoy, Jacques; Liberatore, Anne-Marie; Thurieau, Christophe

PATENT ASSIGNEE(S): Societe de Conseils de Recherches et d'Applications Scientifiques (S.C.R.A.S, Fr.

SOURCE: PCT Int. Appl., 261 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: French

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2001026656	A2	20010419	WO 2000-FR2805		20001010
WO 2001026656	A3	20020418			
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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
FR 2799461	A1	20010413	FR 1999-12643		19991011
FR 2799461	B1	20020104			
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BR 2000014649	A	20020618	BR 2000-14649		20001010
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EP 1228760	A2	20020807	EP 2002-76763		20001010
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NO 2002001689	A	20020530	NO 2002-1689		20020410
US 2004132788	A1	20040708	US 2003-681002		20031008
PRIORITY APPLN. INFO.:			FR 1999-12643	A	19991011
			FR 2000-10151	A	20000801
			FR 2000-11169	A	20000901
			EP 2000-967988	A3	20001010
			EP 2002-76763	A3	20001010
			WO 2000-FR2805	W	20001010
			JP 1989-4943	A	20010410
			JP 1990-1811	A	20020214
			US 2002-89993	A2	20020404

OTHER SOURCE(S): MARPAT 134:311210

AN 2001:283789 CAPLUS

DN 134:311210

ED Entered STN: 20 Apr 2001

TI 5-Membered heterocycle derivatives useful as monoamine oxidase inhibitors, lipid peroxidation inhibitors, and sodium channel modulators, and the production thereof, and use thereof as medicaments

IN Chabrier de Lassauniere, Pierre-Etienne; Harnett, Jeremiah; Bigg, Dennis; Pommier, Jacques; Lannoy, Jacques; Liberatore, Anne-Marie; Thurieau, Christophe

PA Societe de Conseils de Recherches et d'Applications Scientifiques (S.C.R.A.S, Fr.

SO PCT Int. Appl., 261 pp.
CODEN: PIXXD2

DT Patent

LA French

IC ICM A61K031-426
ICS A61K031-421; A61K031-42; A61K031-4164; A61K031-417; A61P025-00; C07D277-28; C07D233-64; C07D261-04; C07D263-32; C07D277-24; C07D417-04; C07D403-06; C07D403-14; C07D413-06; C07D417-06; C07D409-06; C07D405-06

CC 28-9 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 63

FAN.CNT 2

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     FR 2799461             B1     20020104
     FR 2812546             A1     20020208    FR 2000-10151          20000801
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     US 2004132788          A1     20040708    US 2003-681002         20031008
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     FR 2000-10151          A      20000801
     FR 2000-11169          A      20000901
     EP 2000-967988         A3     20001010
     EP 2002-76763          A3     20001010
     WO 2000-FR2805         W      20001010
     JP 1989-4943           A      20010410
     JP 1990-1811           A      20020214
     US 2002-89993          A2     20020404
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                         A61P025-00; C07D277-28; C07D233-64; C07D261-04;
                         C07D263-32; C07D277-24; C07D417-04; C07D403-06;
                         C07D403-14; C07D413-06; C07D417-06; C07D409-06;
                         C07D405-06
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                         C07D277/24; C07D277/28; C07D403/04+239B+233+209C;
                         C07D405/06+319+233; C07D409/06+333+233;
                         C07D413/06+263B+209C; C07D417/04+27+277B;
                         C07D417/04+277B+209C
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                         C07D277/28; C07D403/04+239B+233+209C;
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                         C07D417/04+277B+209; C07D417/04+277B+209C;
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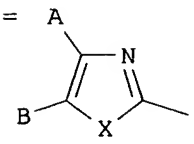
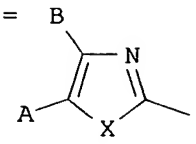
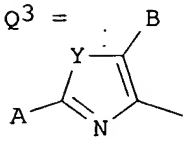
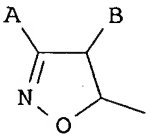
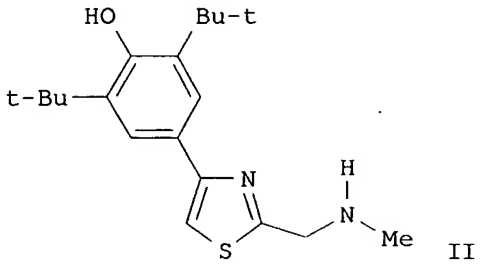
Q1 = 

Q2 = 

Q3 = 

Q4 = 



II

AB The invention relates to pharmaceutical use of heterocyclic compds. of general formula Het(A)(B)-(CH2)n-CR1R2-Q [I; wherein the substituted heterocyclic ring Het(A)(B) = Q1-Q4; A = various aryl or heteroaryl systems, especially a substituted Ph or biphenyl radical, or also alkyl, cycloalkyl, or cycloalkylalkyl; B = especially H or alkyl, or also aryl or substituted alkyl; X = especially NH or S, or also substituted NH; Y = O or S; n = 0-6; R1, R2 = especially H, alkyl, or cycloalkyl; Q = NR3R4 or OR5; R3 and R4 = especially H, alkyl, cycloalkyl, alkynyl, cyanoalkyl alkoxycarbonyl, aralkoxycarbonyl or (cycloalkyl)oxycarbonyl; R5 = H, alkyl, alkynyl, or cyanoalkyl]. I and their racemates, enantiomers, and/or salts can be used for producing medicaments for inhibiting monoamine oxidases (MAO), inhibiting lipid peroxidn., and/or for acting as modulators of sodium channels. The resulting medicaments are particularly for use in treating Parkinson's disease, senile dementia, Alzheimer's disease, Huntington's chorea, amyotrophic lateral sclerosis, **schizophrenia**, depression, psychosis, pain and epilepsy. Approx. 350 synthetic examples of I and their salts are given, and numerous free bases of I are claimed. For instance, protection of sarcosinamide-HCl with BOC anhydride gave 72% BOC-N(Me)CH2CONH2, which was converted to the thioamide with (P2S5)2 in 65% yield. Cyclocondensation of the thioamide with 2-bromo-1-(3,5-di-tert-butyl-4-hydroxyphenyl)ethanone (28%), followed by deprotection (73%) and salification (92%), gave thiazole derivative II as the HCl salt. II inhibited binding of the MAO-B specific ligand [3H]-Ro-19-6327 to rat mitochondrial prepns. with IC50 < 10 μM. Selected I also inhibited formation of malondialdehyde by lipid peroxidn. in rat cerebral cortex prepns., and inhibited specific binding of [3H]-batrachotoxin to voltage-dependent sodium channels in rat cerebral cortex homogenates.

ST heterocycle prepn inhibitor monoamine oxidase lipid peroxidn sodium channel; sodium channel modulator MAO inhibitor oxazole thiazole imidazole isoxazoline

IT Nervous system
(Huntington's chorea, treatment of; preparation of five-membered heterocycle

yl]ethanone 109183-71-3, (S)-N-(tert-Butoxycarbonyl)cyclohexylglycine 175204-79-2, 2-(tert-Butylcarbonyloxy)thioacetamide 214541-02-3, Ethyl 3',5'-di-tert-butyl-4'-hydroxy-[1,1'-biphenyl]-4-carboxylate 218944-58-2, tert-Butyl (2-amino-2-thioxoethyl)(methyl)carbamate 335247-36-4, (1R)-1-(1-Benzyl-4-tert-butyl-1H-imidazol-2-yl)-2-(1H-indol-3-yl)ethanamine 335247-37-5, [4-[1,1'-Biphenyl]-4-yl-1H-imidazol-2-yl]-N-methylmethanamine
RL: RCT (Reactant); RACT (Reactant or reagent)
(precursor; preparation of five-membered heterocycle derivs. as MAO inhibitors, lipid peroxidn. inhibitors, and sodium channel modulators)

L28 ANSWER 21 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:900625 CAPLUS
DOCUMENT NUMBER: 134:56689
TITLE: Preparation of pyrazinyl phenoxyethyl ethers as 5-HT2C receptor modulators
INVENTOR(S): Nilsson, Bjorn; Tejbrant, Jan; Pelcman, Benjamin; Ringberg, Erik; Thor, Markus; Nilsson, Jonas; Jonsson, Mattias
PATENT ASSIGNEE(S): Pharmacia & Upjohn AB, Swed.
SOURCE: PCT Int. Appl., 151 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000076984	A2	20001221	WO 2000-SE1017	20000519
WO 2000076984	A3	20010208		
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NO 2001005686	A	20020115	NO 2001-5686	20011121
PRIORITY APPLN. INFO.:			SE 1999-1884	A 19990521
			US 1999-137527P	P 19990603
			WO 2000-SE1017	W 20000519

OTHER SOURCE(S): MARPAT 134:56689
AN 2000:900625 CAPLUS
DN 134:56689
ED Entered STN: 22 Dec 2000
TI Preparation of pyrazinyl phenoxyethyl ethers as 5-HT2C receptor modulators
IN Nilsson, Bjorn; Tejbrant, Jan; Pelcman, Benjamin; Ringberg, Erik; Thor, Markus; Nilsson, Jonas; Jonsson, Mattias
PA Pharmacia & Upjohn AB, Swed.
SO PCT Int. Appl., 151 pp.
CODEN: PIXXD2
DT Patent

LA English
IC ICM C07D241-18
ICS C07D241-20; C07D405-12; A61K031-497; A61P025-00
CC 28-17 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 63
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
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OS MARPAT 134:56689
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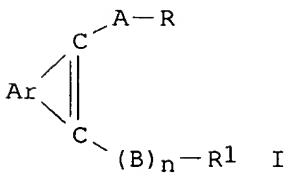

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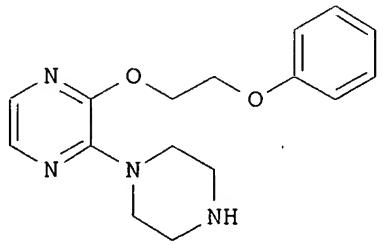

II

AB The title compds. (I) [wherein Ar = (un)substituted (hetero)aryl; A = O, S, SO2, NH, alkyl- or acyl-substituted N, or (un)saturated, (un)substituted (hetero)alkylene chain which may contain a bridge to form a ring; B = CR4R5, OCR4R5, NR6CR4R5, NR6O, S, or SO2; R = (un)substituted cycloalkyl or (hetero)aryl; R1 = (un)saturated (amino)azacyclic or saturated (amino)diazacyclic, (amino)azabicyclic, or diazabicyclic ring, or (CR4R5)xNR2aR3a; n = 0-1; R2a and R3a = independently H, Me, or Et, or taken together with the N to which they are bound form a pyrrolidine, piperazine, or **morpholine** ring; R4, R5, and R6 = independently H

or alkyl; x = 2-4] and their pharmaceutically acceptable salts were prepared and tested as 5-HT2C receptor modulators. Examples include 235 syntheses, a tablet formulation, and pharmacol. tests. For instance, 2,3-dichloropyrazine and 2-phenoxyethanol were treated with t-BuONa in dioxane to give 2-chloro-3-(2-phenoxyethoxy)pyrazine (62%). The halopyrazine, piperazine, and K2CO3 in MeCN were stirred and heated to afford the desired 2-(phenoxy)ethyl 3-(1-piperazinyl)-2-pyrazinyl ether (II) in 65% yield, which was then converted to the maleate salt. In an affinity assay using membranes prepared from a transfected HEK293 cell line stably expressing the 5-HT2C receptor protein, I typically exhibited 5HT2C receptor affinity values (K1) ranging from 1 nM to 1500 nM. Specific values ranging from 5 nM to 377 nM were reported for 12 compds. Agonist efficacy at the 5-HT2C receptor for I were determined by the ability of the compds. to mobilize intracellular Ca in transfected HEK293 cells, and typical maximum responses of the agonists were in the range of 20-100% relative to the maximum response of 5-HT (serotonin) at a concentration of 1 μM.

Acute toxicity studies in mice following oral administration of I showed that mortality typically occurred at doses between 200 mg/kg to 450 mg/kg body weight I are useful for the treatment of serotonin-related disorders, such as eating disorders, especially obesity, memory disorders, **schizophrenia**, mood disorders, anxiety disorders, pain, sexual dysfunctions, and urinary disorders (no data).

ST pyrazinyl phenoxyethoxy ether prepn serotonin receptor modulator; phenoxyethoxy pyrazinyl ether prepn antiobesity antidepressant analgesic; ether pyrazinyl phenoxyethoxy prepn sexual dysfunction urinary disorder treatment

IT 5-HT receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study); PROC (Process)
(5-HT2C; preparation of hetercyclylpyrazinyl phenoxyethoxy ether 5-HT2C receptor modulators by coupling of phenoxyethanols with 2,3-dichloropyrazine followed by addition of heterocycles)

IT Mental disorder
(affective, seasonal, treatment; preparation of hetercyclylpyrazinyl phenoxyethoxy ether 5-HT2C receptor modulators by coupling of phenoxyethanols with 2,3-dichloropyrazine followed by addition of heterocycles)

IT Mental disorder
(depression, major, treatment; preparation of hetercyclylpyrazinyl phenoxyethoxy ether 5-HT2C receptor modulators by coupling of phenoxyethanols with 2,3-dichloropyrazine followed by addition of heterocycles)

IT Memory, biological
Sexual behavior
(disorder, treatment; preparation of hetercyclylpyrazinyl phenoxyethoxy ether 5-HT2C receptor modulators by coupling of phenoxyethanols with 2,3-dichloropyrazine followed by addition of heterocycles)

IT Bladder
(incontinence, treatment; preparation of hetercyclylpyrazinyl phenoxyethoxy ether 5-HT2C receptor modulators by coupling of phenoxyethanols with 2,3-dichloropyrazine followed by addition of heterocycles)

IT Mental disorder
(manic bipolar disorder, treatment; preparation of hetercyclylpyrazinyl phenoxyethoxy ether 5-HT2C receptor modulators by coupling of phenoxyethanols with 2,3-dichloropyrazine followed by addition of heterocycles)

IT Analgesics
Antidepressants
Antiobesity agents
Anxiolytics
(preparation of hetercyclylpyrazinyl phenoxyethoxy ether 5-HT2C receptor modulators by coupling of phenoxyethanols with 2,3-dichloropyrazine

followed by addition of heterocycles)

IT **Schizophrenia**
(treatment; preparation of hetercyclylpyrazinyl phenoxyethoxy ether 5-HT2C receptor modulators by coupling of phenoxyethanols with 2,3-dichloropyrazine followed by addition of heterocycles)

IT 313653-94-0P, 2-(Phenoxy)ethyl 3-(1-piperazinyl)-2-pyrazinyl ether 313653-97-3P, 2-(2-Furylmethoxy)-3-(1-piperazinyl)pyrazine 313654-02-3P, 2-(2-Phenoxyethoxy)-3-(1-piperazinyl)quinoxaline 313654-38-5P, 4-[2-[[3-(1-Piperazinyl)-2-pyrazinyl]oxy]ethoxy]-1,3-benzoxazol-2-amine 313654-74-9P, N-Methyl-N-(2-phenoxyethyl)-3-(1-piperazinyl)-2-pyrazinamine 313655-29-7P, 8-[2-[[3-(1-Piperazinyl)-2-pyrazinyl]oxy]ethoxy]quinazoline 313655-66-2P, N-Phenyl-3-[2-[[3-(1-piperazinyl)-2-pyrazinyl]oxy]ethoxy]aniline 313655-69-5P, [3-[2-[[3-(1-Piperazinyl)-2-pyrazinyl]oxy]ethoxy]phenyl]methanol Maleate 313655-74-2P, 2-[2-[3-(Methoxymethyl)phenoxy]ethoxy]-3-(1-piperazinyl)pyrazine 313655-77-5P, 3-[2-[[3-(1-Piperazinyl)-2-pyrazinyl]oxy]ethoxy]benzamide 313655-79-7P, N-Phenyl-4-(2-[[3-(1-piperazinyl)-2-pyrazin]oxy]ethoxy)aniline 313655-82-2P, 2-(1-Piperazinyl)-3-[2-[3-(trifluoromethoxy)phenoxy]ethoxy]pyrazine 313655-90-2P, 2-[2-(3-Butoxyphenoxy)ethoxy]-3-(1-piperazinyl)pyrazine 313655-93-5P, 2-[2-(3-Trifluoromethylphenoxy)ethoxy]-3-(1-piperazinyl)pyrazine 313655-94-6P, 2-[2-([1,1'-Biphenyl]-3-yloxy)ethoxyl-3-(1-piperazinyl)pyrazine 313655-99-1P, 2-[4-[2-[[3-(1-Piperazinyl)-2-pyrazinyl]oxy]ethoxy]phenoxy]ethanol 313656-01-8P, 2-[3-(2-[[3-(1-Piperazinyl)-2-pyrazinyl]oxy]ethoxy)phenoxy]ethanol 313656-25-6P, 2-(5-Isoquinolinyloxy)ethyl 3-(1-piperazinyl)-2-pyrazinyl ether 313656-30-3P, 2-(5-Quinolinyloxy)ethyl 3-(1-piperazinyl)-2-pyrazinyl ether 313656-43-8P, 2-(Benzofuran-7-yloxy)ethyl 3-(1-piperazinyl)-2-pyrazinyl ether 313656-74-5P, 2-(2,3-Dihydro-2,2-dimethyl-7-benzofuranyloxy)ethyl 3-(1-piperazinyl)-2-pyrazinyl ether 313656-76-7P, 2-(1,3-Benzoxazol-4-yloxy)ethyl 3-(1-piperazinyl)-2-pyrazinyl ether 313656-81-4P, 4-[2-[[3-(1-Piperazinyl)-2-pyrazinyl]oxy]ethoxy]-2-quinolinamine 313656-86-9P, 2-[2-(3-Pyridinyloxy)ethoxy]-3-(1-piperazinyl)quinoxaline 313656-92-7P, 2-[2-(3-Pyridinyloxy)ethoxy]-3-(1-piperazinyl)-6,7-dichloroquinoxaline 313657-07-7P, 2-(2-Phenoxy)ethyl 3-(2-methyl-1-piperazinyl)-2-pyrazinyl ether 313657-54-4P, 2-(2,3-Dihydrobenzofuran-7-yloxy)ethyl 3-(1-piperazinyl)-2-pyrazinyl ether 313657-59-9P, 5-Bromo-2-(1-piperazinyl)-3-[2-(3-pyridinyloxy)ethoxy]pyrazine 313657-65-7P, 2-[2-[(3-Methoxy-2-pyrazinyl)oxy]ethoxy]-3-(1-piperazinyl)pyrazine 313657-69-1P, 2-[2-[(2-Methoxy-3-pyridinyl)oxy]ethoxy]-3-(1-piperazinyl)pyrazine 313657-73-7P, (2R)-1-[3-[2-[(2-Methoxy-3-pyridinyl)oxy]ethoxy]-2-pyrazinyl]-2-methylpiperazine 313657-97-5P, 5-Ethoxy-3-pyridinyl 2-[[3-((2R)-2-methylpiperazinyl)-2-pyrazinyl]oxy]ethyl ether 313658-00-3P, 3-((2R)-2-Methylpiperazinyl)-2-pyrazinyl 2-(5-pyrimidinyloxy)ethyl ether 313658-03-6P, 2-[2-[(6-Chloro-3-pyridinyl)oxy]ethoxy]-3-(1-piperazinyl)pyrazine 313658-05-8P, 2-[2-[(6-Methoxy-3-pyridinyl)oxy]ethoxy]-3-(1-piperazinyl)pyrazine 313658-14-9P, 3-(1-Piperazinyl)-2-pyrazinyl 1,2,3,4-tetrahydro-2-naphthalenylmethyl ether 313658-16-1P, 3-((2R)-2-Methylpiperazinyl)-2-pyrazinyl 1,2,3,4-tetrahydro-2-naphthalenylmethyl ether 313658-60-5P, 2-[2-[3-(2-Methoxyethoxy)phenoxyl]ethoxy]-3-(1-piperazinyl)pyrazine
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of hetercyclylpyrazinyl phenoxyethoxy ether 5-HT2C receptor modulators by coupling of phenoxyethanols with 2,3-dichloropyrazine followed by addition of heterocycles)

IT 313653-98-4P, 2-(2-Furylmethoxy)-3-(1-piperazinyl)pyrazine Maleate 313654-00-1P 313654-04-5P, 2-[2-(2-Naphthyloxy)ethoxy]-3-(1-piperazinyl)pyrazine Trifluoroacetate 313654-07-8P, 2-(4-Bromophenoxy)ethyl 3-(1-piperazinyl)-2-pyrazinyl ether Trifluoroacetate

313658-13-8P, 2-(2,5-Dimethoxyphenoxy)-1-ethanol 313658-20-7P, 3-Chloro-4-(1-piperazinyl)-1,2,5-thiadiazole 313658-22-9P, tert-Butyl 4-[3-[2-(2,3-Dihydro-1,4-benzodioxin-6-yloxy)ethoxy]-2-pyrazinyl]-1-piperazinecarboxylate 313658-32-1P, tert-Butyl (3R)-3-methyl-4-[3-[2-(3-pyridinyloxy)ethoxy]-2-pyrazinyl]-1-piperazinecarboxylate 313658-37-6P, tert-Butyl 4-[3-[(2-hydroxyethyl)sulfanyl]-2-pyrazinyl]-1-piperazinecarboxylate 313658-38-7P, tert-Butyl 4-[3-[(2-phenoxyethyl)sulfanyl]-2-pyrazinyl]-1-piperazinecarboxylate 313658-40-1P, tert-Butyl 4-[4-(2-hydroxyethoxy)-1,2,5-thiadiazol-3-yl]-1-piperazinecarboxylate 313658-41-2P, tert-Butyl 4-[4-[2-[(2-oxo-2H-chromen-7-yl)oxy]ethoxy]-1,2,5-thiadiazol-3-yl]-1-piperazinecarboxylate 313658-42-3P, tert-Butyl 4-[4-[2-(7-isoquinolinyloxy)ethoxy]-1,2,5-thiadiazol-3-yl]-1-piperazinecarboxylate 313658-46-7P, tert-Butyl 4-[3-[2-(3-hydroxyphenoxy)ethoxy]-2-pyrazinyl]-1-piperazinecarboxylate 313658-62-7P, tert-Butyl 4-[3-[2-[3-(2-methoxyethoxy)phenoxy]ethoxy]-2-pyrazinyl]-1-piperazinecarboxylate
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of hetercyclylpyrazinyl phenoxyethoxy ether 5-HT2C receptor modulators by coupling of phenoxyethanols with 2,3-dichloropyrazine followed by addition of heterocycles)

IT 313653-95-1P, 2-(Phenoxy)ethyl 3-(1-piperazinyl)-2-pyrazinyl ether Maleate
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of hetercyclylpyrazinyl phenoxyethoxy ether 5-HT2C receptor modulators by coupling phenoxyethanols with 2,3-dichloropyrazine followed by addition of heterocycles)

=> log y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	258.26	258.89

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-39.90	-39.90

STN INTERNATIONAL LOGOFF AT 23:07:34 ON 12 DEC 2004

12/12/04 10/764,853

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.42	0.42

FILE 'REGISTRY' ENTERED AT 22:06:50 ON 12 DEC 2004
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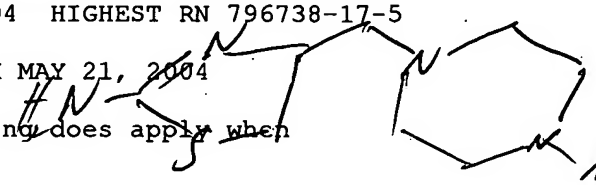
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

// Structure Search piperazine deriv

STRUCTURE FILE UPDATES: 10 DEC 2004 HIGHEST RN 796738-17-5
DICTIONARY FILE UPDATES: 10 DEC 2004 HIGHEST RN 796738-17-5



TSCA INFORMATION NOW CURRENT THROUGH MAY 21, 2004

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

but - only in the app

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

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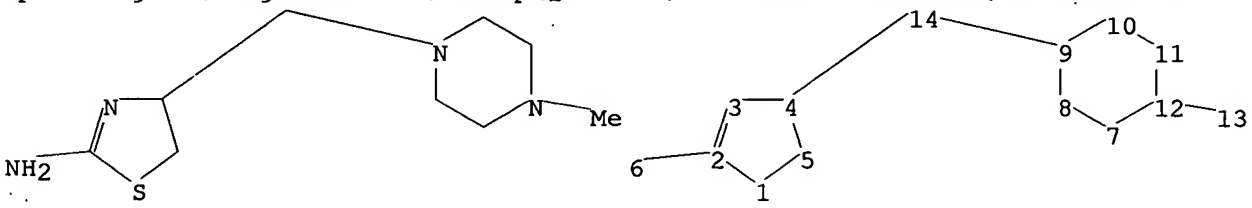

chain nodes :
6 13 14
ring nodes :
1 2 3 4 5 7 8 9 10 11 12
chain bonds :
2-6 4-14 9-14 12-13
ring bonds :
1-2 1-5 2-3 3-4 4-5 7-8 7-12 8-9 9-10 10-11 11-12
exact/norm bonds :
1-2 1-5 2-3 2-6 3-4 4-5 7-8 7-12 8-9 9-10 9-14 10-11 11-12
exact bonds :
4-14 12-13

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:CLASS 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 13:CLASS 14:CLASS

L1 STRUCTURE UPLOADED

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L1 HAS NO ANSWERS
L1                STR
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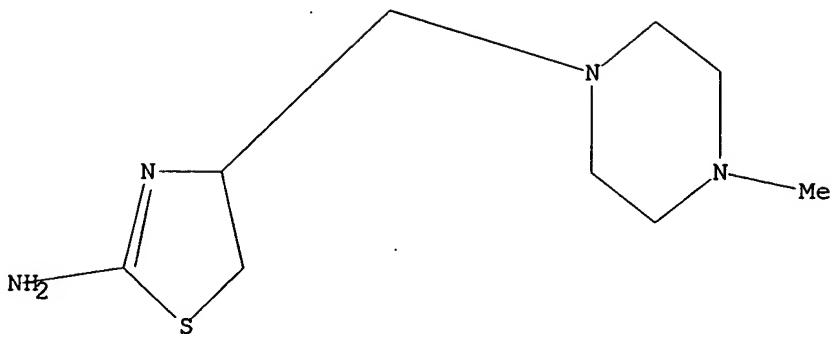


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Structure attributes must be viewed using STN Express query preparation.


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SAMPLE SEARCH INITIATED 22:07:12 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -     94 TO ITERATE

100.0% PROCESSED      94 ITERATIONS                                0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:          1299 TO     2461
PROJECTED ANSWERS:                0 TO        0

L2             0 SEA SSS SAM L1

=> s L1 full
FULL SEARCH INITIATED 22:07:18 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -   1943 TO ITERATE

100.0% PROCESSED    1943 ITERATIONS                               2 ANSWERS
SEARCH TIME: 00.00.01

L3             2 SEA SSS FUL L1

=> d L3 1-2 ti
'TI' IS NOT A VALID FORMAT FOR FILE 'REGISTRY'

The following are valid formats:

Substance information can be displayed by requesting individual
fields or predefined formats.  The predefined substance formats
are:  (RN = CAS Registry Number)

REG     - RN
SAM     - Index Name, MF, and structure - no RN
FIDE    - All substance data, except sequence data
IDE     - FIDE, but only 50 names
SQIDE   - IDE, plus sequence data
SQIDE3  - Same as SQIDE, but 3-letter amino acid codes are used
SQD     - Protein sequence data, includes RN
SQD3    - Same as SQD, but 3-letter amino acid codes are used
SQN     - Protein sequence name information, includes RN
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CALC - Table of calculated properties
EPROP - Table of experimental properties
PROP - EPROP and CALC

Any CA File format may be combined with any substance format to obtain CA references citing the substance. The substance formats must be cited first. The CA File predefined formats are:

ABS -- Abstract
APPS -- Application and Priority Information
BIB -- CA Accession Number, plus Bibliographic Data
CAN -- CA Accession Number
CBIB -- CA Accession Number, plus Bibliographic Data (compressed)
IND -- Index Data
IPC -- International Patent Classification
PATS -- PI, SO
STD -- BIB, IPC, and NCL

IABS -- ABS, indented, with text labels
IBIB -- BIB, indented, with text labels
ISTD -- STD format, indented

OBIB -------- AN, plus Bibliographic Data (original)
OIBIB ------- OBIB, indented with text labels

SBIB -------- BIB, no citations
SIBIB ------- IBIB, no citations

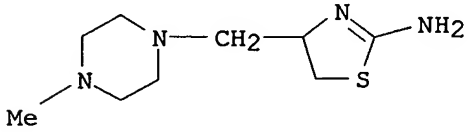
The ALL format gives FIDE BIB ABS IND RE, plus sequence data when it is available.
The MAX format is the same as ALL.
The IALL format is the same as ALL with BIB ABS and IND indented, with text labels.

For additional information, please consult the following help messages:

HELP DFIELDS -- To see a complete list of individual display fields.
HELP FORMATS -- To see detailed descriptions of the predefined formats.
ENTER DISPLAY FORMAT (IDE):end

=> d scan

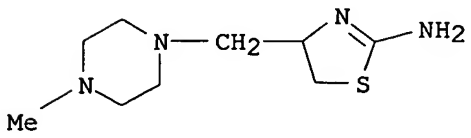
L3 2 ANSWERS REGISTRY COPYRIGHT 2004 ACS on STN
IN 2-Thiazolamine, 4,5-dihydro-4-[(4-methyl-1-piperazinyl)methyl]- (9CI)
MF C9 H18 N4 S
CI COM



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):1

L3 2 ANSWERS REGISTRY COPYRIGHT 2004 ACS on STN
IN 2-Thiazolamine, 4,5-dihydro-4-[(4-methyl-1-piperazinyl)methyl]-, trihydrochloride (9CI)
MF C9 H18 N4 S . 3 Cl H



●3 HCl

ALL ANSWERS HAVE BEEN SCANNED

=> fil caplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	155.84	156.26

FILE 'CAPLUS' ENTERED AT 22:07:58 ON 12 DEC 2004
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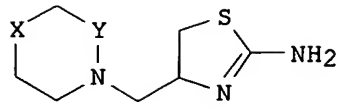
FILE COVERS 1907 - 12 Dec 2004 VOL 141 ISS 25
FILE LAST UPDATED: 10 Dec 2004 (20041210/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s L3
L4 1 L3

=> d L4 abs ibib hitstr

L4 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2004 ACS on STN
GI



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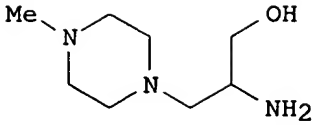
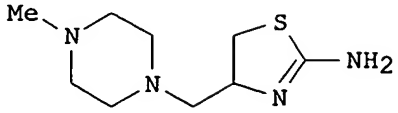


II



III

AB The invention concerns the use of 2-aminothiazoline derivs. I or their pharmaceutically acceptable salts as inhibitors of inducible NO-synthase, i.e., NOS-2 [wherein: (a) Y = CH2 and X = O, NH, N-alkyl, N-CH2Ph, N-Ph, N-(2-pyridyl), N-(3-pyridyl), N-(4-pyridyl), N-(2-pyrimidyl), N-(5-pyrimidyl), S, SO, SO2, CH2, or CHPh; or (b) Y = CO and X = NH, N-Ph, N-(2-pyridyl), N-(3-pyridyl), N-(4-pyridyl), N-(2-pyrimidyl), N-(5-pyrimidyl)]. A 5-step preparation of one example is given, plus 3 standard formulations. Thus, addition reaction of N-methylpiperazine with Me 2-acetamidoacrylate, reduction of the obtained ester to an alc., and hydrolysis of the amide function with aqueous HCl, gave 2-amino-3-(4-methylpiperazin-1-yl)-1-propanol (II) as the HCl salt. The latter was N-thiocarbamoylated with tert-Bu isothiocyanate, and cyclized to a thiazoline in aqueous HCl, to give invention compound III as the trihydrochloride. I were tested against rat or mouse NOS-2, and recombinant bovine NOS-3. I had IC50 values ≤ 10 μM against NOS-2, with a selectivity (IC50 NOS-3/NOS-2) > 45. The toxicities of I are weak, with LD50 > 40 mg/kg s.c. in mice.

ACCESSION NUMBER: 2003:376836 CAPLUS
DOCUMENT NUMBER: 138:368886
TITLE: Preparation of 4-(azinylmethyl)-substituted 2-aminothiazoline derivatives as inhibitors of inducible NO-synthase and their use in the treatment of Parkinson's disease
INVENTOR(S): Bigot, Antony; Carry, Jean-Christophe; Mignani, Serge
PATENT ASSIGNEE(S): Aventis Pharma S.A., Fr.
SOURCE: PCT Int. Appl., 26 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003040115	A1	20030515	WO 2002-FR3810	20021107

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG